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THE YEAR BOOK PUBLISHERS, INC. 200 East Illinois St., Chicago 11, Ill.

31 January 1958, Volume 127, Number 3292

SCIENCE

CURRENT PROBLEMS IN RESEARCH

Superfluids

K. Mendelssohn

For quite a long time experiments at low temperatures were aimed at reaching the absolute zero. Absolute zero, as such, is a rather old concept. Two hundred and fifty years ago Amontons had already visualized some state of matter at which all motion would come to rest, and which thereby would constitute a lower limit to our temperature scale. The concept of the ultimate cessation of molecular motion was maintained in this form for quite some time, until 50 years ago, when Nernst, by enunciating the third law of thermodynamics, somewhat modified it by substituting for the zero point of energy the zero point of entropy.

Entropy is a concept which many people consider "difficult." Even scientists dislike it sometimes, but, after all, it is not such an abstract thing. It simply measures the degree of disorder in any physical system. Thus, with the advent of the third law of thermodynamics, a change occurred in the approach to absolute zero as the approach to complete order, and not, as it was thought formerly, to complete rest. At the same time, the third law of thermodynamics contained the provision that absolute zero could not be reached by any physical process, and thereby the emphasis of research has been shifted to the question of approach rather than the question of attainment of a final point in the temperature scale.

Recent low-temperature research has therefore been directed toward better understanding of the state of ultimate order rather than that of ultimate rest in matter. As such, it has revealed aspects which are unique. These strange phenomena, which have now been classed under the general term *superfluids,* have no counterpart in the observational world of everyday physics. They stand entirely on their own and, possibly for this reason, have so far resisted theoretical explanation.

It seems quite clear that these phenomena must be related in some way to the amount of energy remaining at absolute zero in any substance—the zero-point energy—or rather to the ratio between zero-point energy and thermal energy. We can expect on the basis of first principles that the region in which the zero-point energy is large compared with the thermal energy will be distinguished as the region in which energy quantization assumes an ever larger part in the aspect of the physical world. In fact, in the phenomena of superfluidity, quantization of energy, which at normal temperatures is restricted to particles of interatomic or perhaps intermolecular size, now transcends into large-scale phenomena, and this is a condition which is alien to our normal observational experience.

Superconductivity

The first of the superfluid phenomena, superconductivity, was discovered by H. Kamerlingh Onnes in Leiden in 1911, three years after the first liquefaction of helium. What Kamerlingh Onnes did was to investigate the dependence of the resistance of a metal on the absolute temperature. At that time there were two different ideas about what the resistance of a metal might do at absolute zero. One school assumed that the resistance should gradually drop to the value zero as zero temperature was approached, whereas the other opinion held that it should rise to infinity. Kamerlingh Onnes used mercury as the first metal to be investigated for the simple reason that he could get it very pure. What he found was rather astonishing. It was so astonishing, in fact, that he had to do a second experiment in order to verify properly the first results. The results showed that the resistance of mercury at first dropped constantly as the temperature was lowered until, at 4°K, it attained an unmeasurably small resistance. It was only in the second experiment, when he had made his method more sensitive, that he found the amazing fact that the resistance, at about 4 degrees, disappeared completely and discontinuously (Fig. 1). This was the first observation of superconductivity, a phenomenon which has since been found in a great number of metals and even in compounds.

If you take a closed ring of a superconductive metal such as lead and induce a current in it, then this current will run for seconds, minutes, days, weeks, months—as long as the ring is kept in liquid helium. Recently it has been shown that the current will run for years without any decrease in its strength. These so-called persistent currents are clearly something that do not occur in ordinary macroscopic physics. A striking way of demonstrating persistent currents is shown in Fig. 2. In a Dewar vessel containing liquid helium, such a current was induced in a set of rings, and a lead sphere was dropped into the system of rings. As the sphere approached the rings, the persistent currents in the rings induced a system of persistent currents on the surface of the sphere. These currents being mutually repellent, the sphere was slowed down in its fall until it came to rest at a position where the mutual repulsion of the currents just counterbalanced the weight of the sphere. There it hung suspended

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in space by this unusual and strange phenomenon. It does not require much imagination or detailed calculation to see that this is a phenomenon which has no counterpart in the other domains of physics.

Figure 3 shows the distribution of the superconductors in the periodic table. For a little while it looked as if they were grouped in two regions in the table, but now other superconductors have been discovered between these regions. One thing seems certain: the monovalent metals are not superconducting. Perhaps a more impressive and slightly more informative diagram can be made when we plot the atomic volume against the atomic number (Fig. 4). Then the superconductors are all contained in a belt which has intermediate atomic volumes. An interesting region of this diagram is the superconducting series, lead, thallium, and mercury. Bismuth is just a bit too large to be a superconductor, and gold is just a bit too small. But if an intermetallic compound of gold and bismuth (Au_2Bi) is made, then this compound will be a superconductor. The case is quite analogous to that of the Heusler alloys in ferromagnetism, where two nonferromagnetic elements will produce a ferromagnetic compound. Here you have two nonsuperconductive parent metals, gold and bismuth, producing a superconductor. This also indicates that superconductivity cannot be a property of the atom, but must be due to some rearrangement of the free electrons in the energy spectrum of the metal. Superconductivity is confined to rather low temperatures, which means that the energy difference is of the order of 10^{-4} electron volts, and it would be difficult to find energy transitions of this order in an individual atom. Figure 5 shows that the transition is connected with an anomaly in the specific heat which by its small absolute size clearly marks it out as an electronic phenomenon.

This very strange and unusual phenomenon of superconductivity has been known for 45 years, and quite a number of attempts have been made to explain it. On the whole, in the intervening years these attempts have averaged three in peacetime and two in wartime per year, but none of them have been very successful. This failure is not due to the fact that we know so little about superconductivity; actually, the trouble is that we know rather too much. Any theory now will have to contain a whole set of phenomena which must all find a consistent explanation. However, before we hazard any opinions on what kind of state the electrons in the metal pass into when the metal becomes superconducting, let us first have a look at the other superfluid, liquid helium itself.

Liquid Helium

Liquid helium was first produced in 1908 by Kamerlingh Onnes, but somehow the discovery of its unusual properties seemed to be dogged by misfortune, or perhaps rather by the fact that people did not quite believe their eyes. The first indication that there was a change in the liquid helium itself at a temperature well below its boiling point was obtained by Dana and Kamerlingh Onnes. They measured the heat of vaporization of helium and found that there was a sort of indentation in the curve for the heat of vaporization against temperature. They also carried out some preliminary specific heat measurements, which, if these had been pursued, would have shown that the difficulty experienced in reaching lower temperatures with helium was due to a large anomaly.

The next indication was found when the density of helium was investigated by Kamerlingh Onnes. The density, as for any ordinary liquid, first increases with falling temperature, but then, at about 2.2 degrees Kelvin, there is a change in the direction of the density curve, and the density decreases again. Helium thus has a density maximum at about 2.2 degrees Kelvin (Fig. 6). There are, of course, other substances, among them water, which have density maxima in the liquid phase, because of some secondary effect. But this sort of explanation became quite untenable when

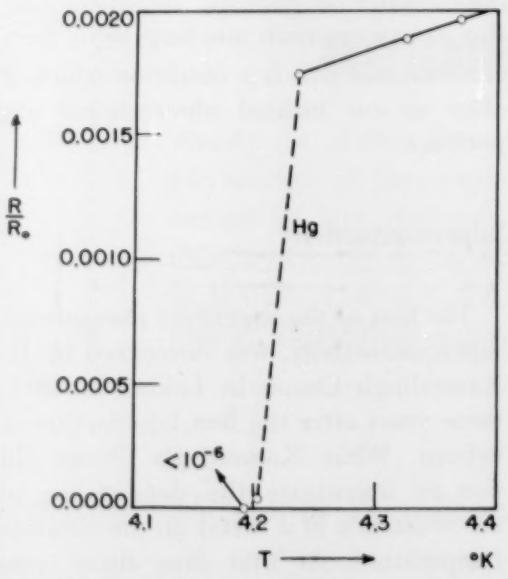

Fig. 1. Kamerlingh Onnes' discovery of superconductivity in mercury.

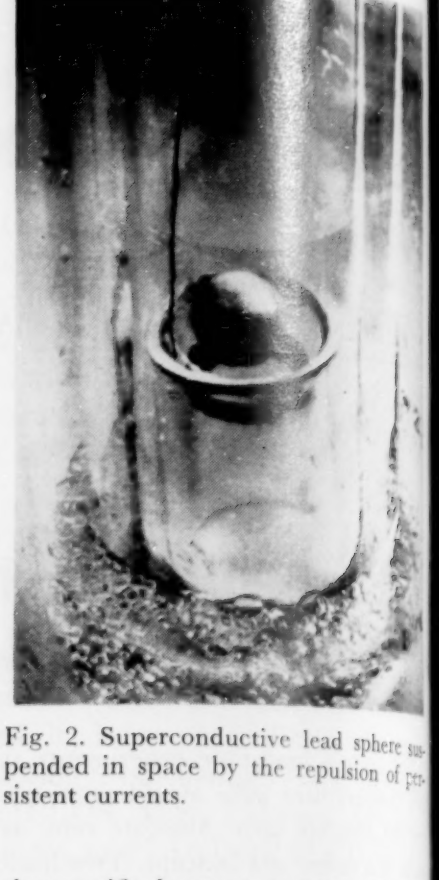

Fig. 2. Superconductive lead sphere suspended in space by the repulsion of persistent currents.

the specific heat was measured by Keesom and Clusius, whose results are shown by Fig. 7. These results led Keesom to the concept of the two states of liquid helium, which are separated from each other by this large anomaly known as the lambda-point. On the basis of these measurements, Keesom proposed to call the form of the liquid below this temperature, helium II, and the one above, helium I. One has to be careful in the term used because it would not be correct to use *phase* or *modification*, for with these terms, one always connects the separation of the forms in space. As is evident from the specific heat curve, there is never a coexistence of helium I and helium II, since there is no latent heat separating the two forms.

For a while the hope remained that there would be a conventional explanation—such as, perhaps, the appearance of liquid crystals—for helium II. Indeed, one has to remember that, owing to its high zero-point energy, helium remains a liquid down to absolute zero. As is clear from Fig. 8, external pressure is required to transform it into the solid phase. Therefore, for a little while the idea was entertained that the anomaly was after all the lost triple-point. Then the x-ray investigations made by Keesom and Taconis showed unmistakably that the form below the lambda-point, helium II, was a liquid showing none of the ordered structure of a solid.

Whereas the helium I, admittedly somewhat gaslike owing to its high zero-

point energy still retains the properties of a liquid or at least those of a reasonably classical aggregate, helium II is quite different. A long time elapsed before this was realized. In retrospect, it seems strange that so many people should have seen and talked about the phenomena in helium below this temperature without having hit upon the correct explanation.

As a bath of liquid helium is cooled by withdrawal of the vapor from above the liquid, the liquid boils vigorously until the lambda-point is reached, when the boiling suddenly stops abruptly. From then on, although one knows from the flow meter that liquid is evaporating, the meniscus stands sharp against the glass wall like the edge of a knife. This phenomenon was quite well known and, while the explanation of it is obvious, it must have appeared very far-fetched. Later on, when Keesom and Miss Keesom made accurate determinations of the heat conductivity, they found indeed that the heat conduction of this dielectric liquid was increasing at this temperature by a factor of about 1 million. This result explained the cessation of boiling immediately, but who would have postulated that a dielectric liquid should suddenly become a substance with the best heat conductivity known, more than a hundred times better than copper or silver. Moreover, it was soon discovered that the heat conductivity of helium II depended on the temperature gradient, on the size of the capillary in which it was measured, on the shape of the vessel, and on other factors. In fact, while there exists high heat flow in liquid helium, the concept of heat *conduction* seems to have lost its meaning.

The same kind of behavior was discovered when the viscosity was investigated. It turned out that the viscosity of liquid helium II also depends on the type of measurement which is used (Fig. 9). A value of about 10^{-5} poise is obtained when an oscillating disk is used as the measuring instrument. If, on the other hand, one uses a Poiseuille method of outflow through narrow channels, the viscosity is less than 10^{-11} poise. Here again is a clear factor of a million between the measured values of the viscosity. Moreover, it was found in a great number of experiments that helium flows through quite narrow channels at a very high rate and largely independent of pressure. This was the discovery of superfluidity. In addition to these phenomena, there exist peculiar thermal effects.

Thermal Effects

If two vessels are connected by a capillary (Fig. 10), and the level of liquid is higher in one vessel than in the other, helium will flow through the capillary toward the lower level, but in doing so the helium below the dropping level will heat up, and the helium below the rising level will cool down. This effect has its exact opposite in that, when one starts with equal levels and supplies heat to one of the reservoirs, the level in the heated vessel will rise, and that in the other vessel will fall. We therefore have a flow of helium from the lower to the higher temperature. This effect can be demonstrated very strikingly, as shown in Fig. 11, by substituting for the capillary a little vessel which

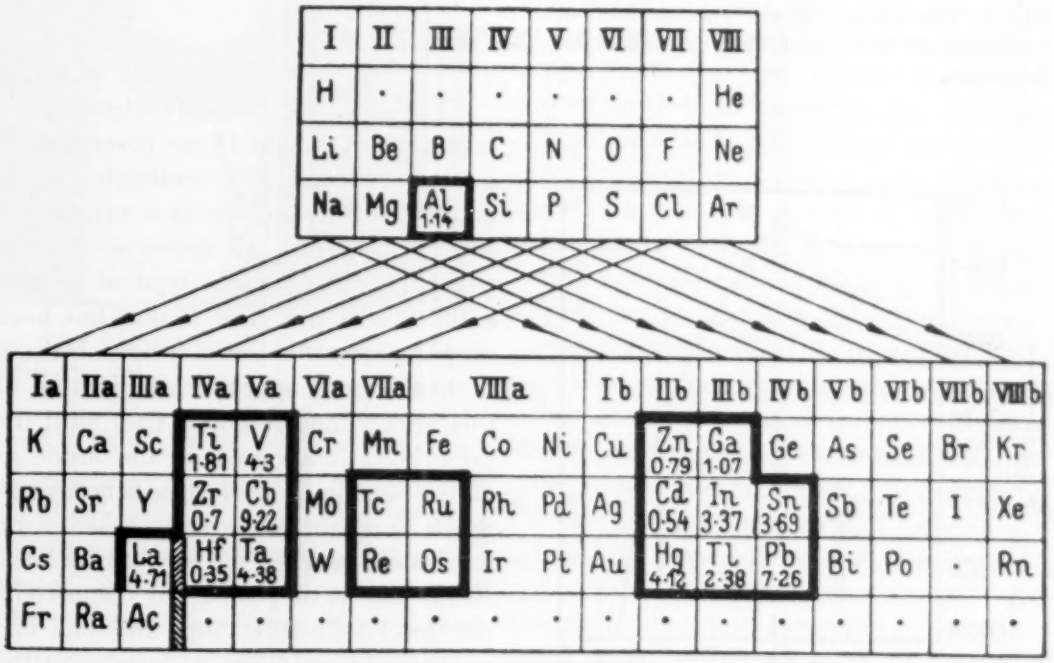
I II III IV V VI VII VIII
H · · · · · · He
Li Be B C N O F Ne
Na Mg Al 1·14 Si P S Cl Ar
Ia IIa IIIa IVa Va VIa VIIa VIIIa Ib IIb IIIb IVb Vb VIb VIIb VIIIb
K Ca Sc Ti 1·81 V 4·3 Cr Mn Fe Co Ni Cu Zn 0·79 Ga 1·07 Ge As Se Br Kr
Rb Sr Y Zr 0·7 Cb 9·22 Mo Tc Ru Rh Pd Ag Cd 0·54 In 3·37 Sn 3·69 Sb Te I Xe
Cs Ba La 4·71 Hf 0·35 Ta 4·38 W Re Os Ir Pt Au Hg 4·12 Tl 2·38 Pb 7·26 Bi Po · Rn
Fr Ra Ac · · · · · · · · · · · · · · · ·
Ce, Pr, Nd, Il, Sm, Eu, Gd, Tb, Dy, Ho, Er, Tm, Yb, Lu
Th, Pa, U, Np, Pu, Am, Cm

Fig. 3. Superconductors in the periodic table.

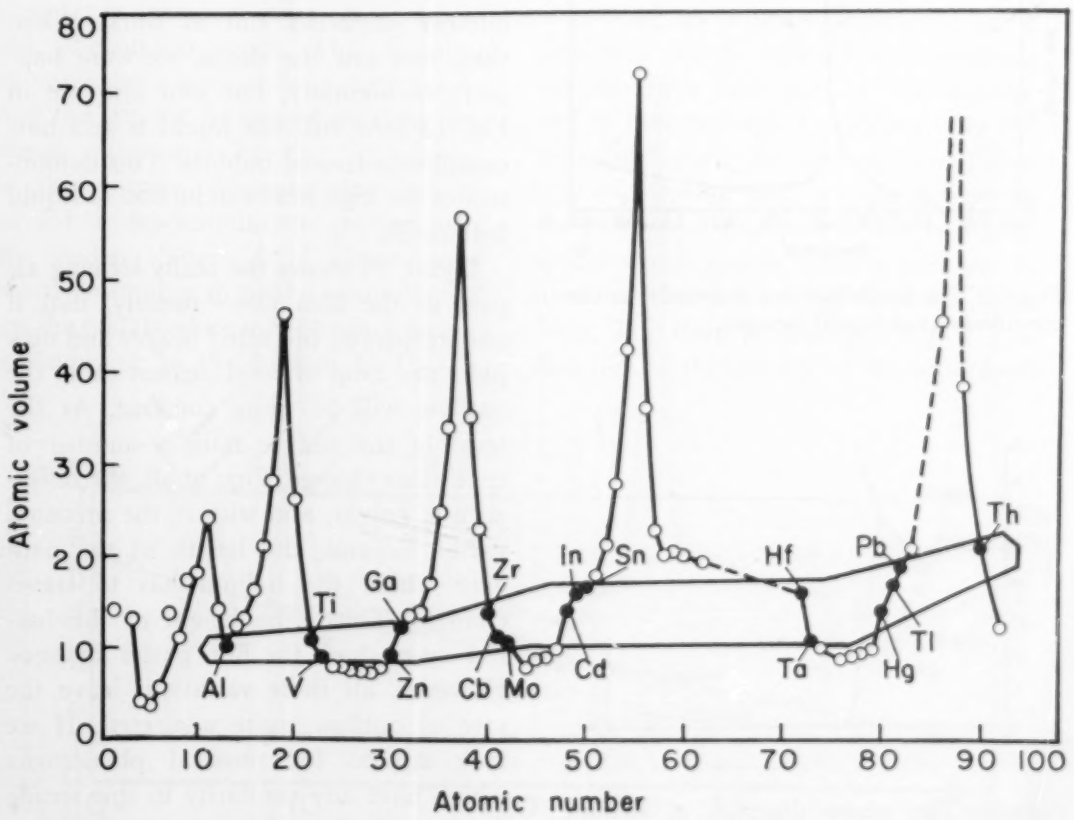

Fig. 4. All superconductors have similar atomic volume.

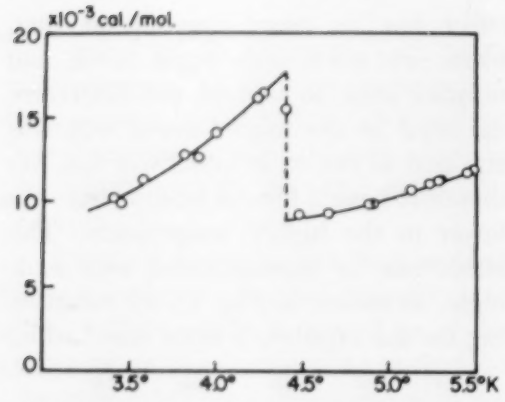

Fig. 5. The change in the specific heat of tantalum at the occurrence of superconductivity.

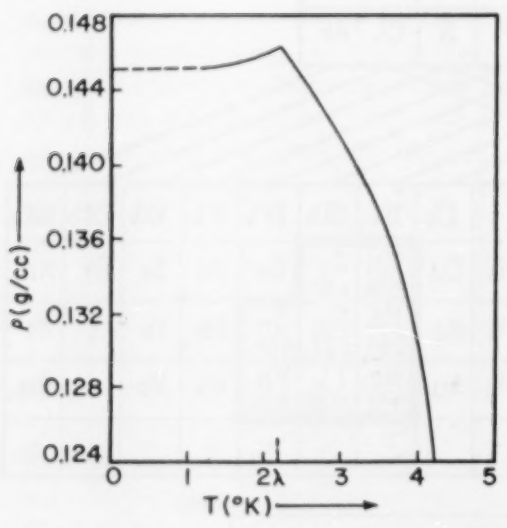

Fig. 6. The density maximum of liquid helium.

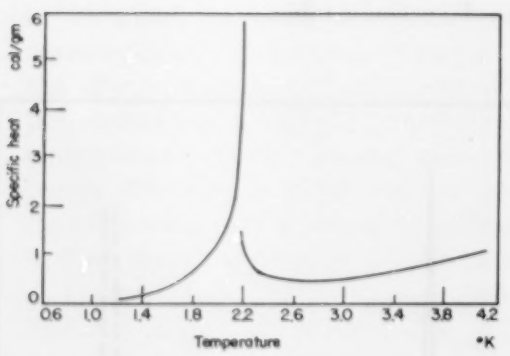

Fig. 7. The lambda-point anomaly in the specific heat of liquid helium.

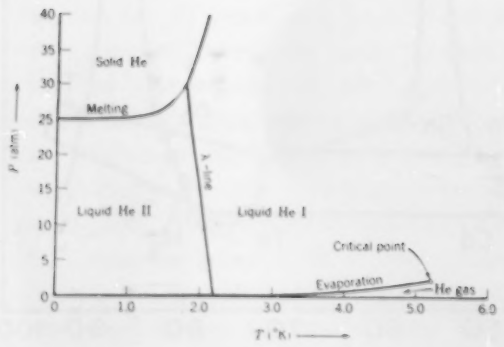

Fig. 8. The phase diagram of helium showing the absence of a triple point.

is open to the helium bath and is filled with powder and which is heated by shining a light on it. The pressure generated by the liquid flow toward the heat will be so high that helium will squirt out in the form of a little fountain. This has become known as the "fountain effect," but it is less confusing to talk about the two thermal effects as the mechanocaloric effect and the thermomechanical effect.

Film Flow

This is not all. All solid substances in contact with helium II are covered with a film of about 10^{-6} centimeter thick, and this film also acts as a vehicle for superflow. Figure 12 shows what happens in a very simple type of experiment. An empty glass beaker has been dipped partly into liquid helium. Helium is then seen to appear in the bottom of this beaker, and it slowly rises until the same level is attained on the inside as on the outside. If the beaker is now withdrawn from the bath, the level will drop until it has reached the level of the bath. If the beaker is pulled out completely, the level will still drop, and one can see little drops of helium forming at the bottom of the beaker and falling back into the bath (Fig. 13). This is the sort of thing that makes one look twice and rub his eyes and wonder whether it is quite true. I remember well the night when we first observed this film transfer. It was well after dinner, and we looked round the building and finally found two nuclear physicists still at work. When they, too, saw the drops, we were happier. Incidentally, one can also see in Fig. 13 how still the liquid is and how completely free of bubbles. This demonstrates the high heat conduction of liquid helium II.

Figure 14 shows the really striking aspect of the film flow—namely, that if one withdraws the filled beaker and now plots the drop of level against time, the outflow will be quite constant. As the level in the beaker falls, a number of conditions change. First of all, the difference in height, and with it, the pressure, varies. Second, the length of the path over which the helium has to travel changes. Third, the height of the barrier over which the film passes changes. However, all these variations leave the rate of outflow quite unaltered. If we look around for physical phenomena which have any similarity to this steady outflow, the best thing we can find is a

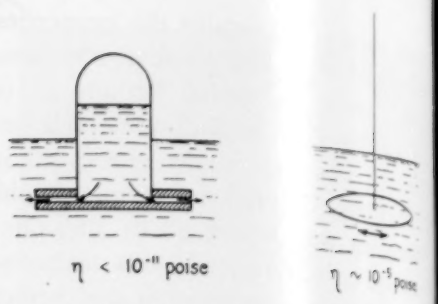

Fig. 9. Different methods of measurement yield different values for the viscosity of liquid helium II: (left) flow through narrow channels; (right) damping of an oscillating disk.

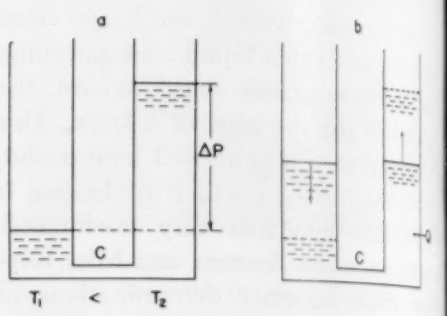

Fig. 10. The (*a*) mechanocaloric and the (*b*) thermomechanical effects.

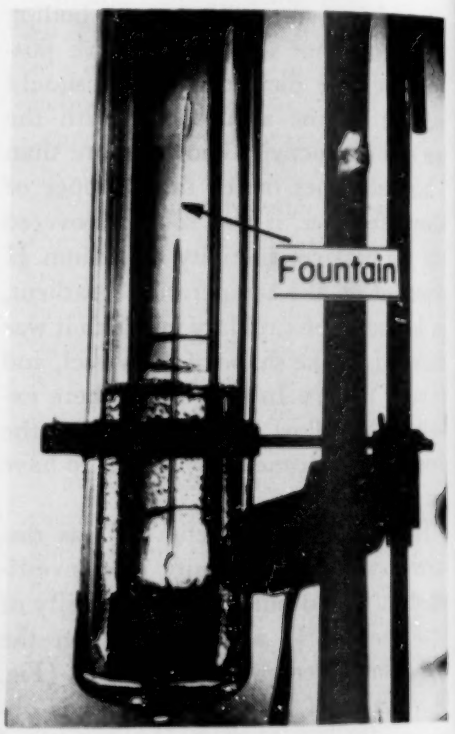

Fig. 11. Helium fountain produced by the thermomechanical pressure.

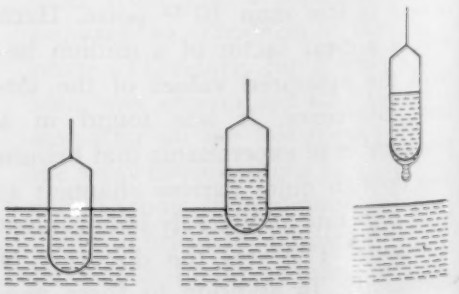

Fig. 12. Film flow of helium II in and out of a glass beaker.

lump of radium in which, uninfluenced by external conditions, the nuclei break up at a given rate, disgorging alpha particles. One is greatly tempted to look at superfluidity in the same way and to regard the outflow simply as the quantum statistical probability of finding a helium atom outside rather than inside the beaker. Whereas the uncertainty principle in the case of the radium atoms does not operate over very large distances, here, as a result of the disproportion between zero-point energy and thermal energy, it will transgress into these large-scale dimensions.

In the case of an individual nucleus of radium, one cannot of course say whether it will explode in the next millionth of a second or will not explode for a hundred million years. All one knows is that, of the large number of atoms in the lump, half will have decayed in 1600 years. I think the same consideration must be applied to the phenomena in helium. One should not try to look at one helium atom as a billiard ball running up one side of the wall and down the other. The helium atoms are wave packets which leak out over the beaker.

In a slight modification of this experiment, superfluidity can be even more clearly demonstrated. Figure 15 shows an arrangement which consists of two beakers placed concentrically into each other. To start with, the level of the helium is the same in both the inner and the outer beaker and in the bath. When the apparatus is lifted out, liquid helium will run from the inner into the outer beaker and from the outer beaker into the bath. What is significant is that there is *no difference in level* between the inner and the outer beakers. The wall of the outer beaker acts as a restricting perimeter to the outflow, and zero potential difference exists between the inner and outer levels. This means that the helium in the film flows completely without friction.

The experiment is the flow counterpart to a well-known electrical phenomenon, namely that of a super current. Figure 16 shows the circuit which is usually employed to find out whether a substance is a superconductor. There is a battery in the circuit with an ammeter, a superconductor, and a limiting resistance which will keep the current below the critical value. Then a voltmeter connected across the superconductor will show zero potential difference. In Fig. 15 the difference in levels between the bath and the inner level

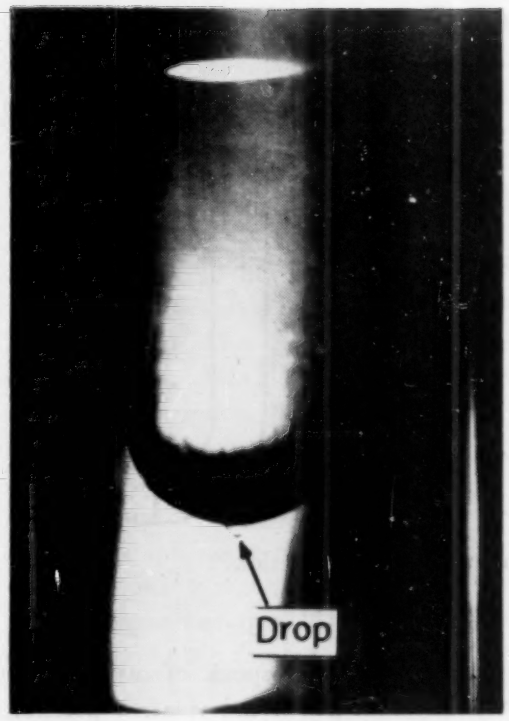

Fig. 13. Liquid drop formed by film transfer.

corresponds to the battery, the outflow rate is the ammeter, the wall of the outer beaker represents the limiting resistance, and the wall of the inner beaker is the superconductor, across which there is zero potential difference.

Entropy

Coming back to our starting point—namely, the postulate that as absolute zero is approached the order in the system increases—we can now ask whether the order is increased when these superfluid phenomena occur. The question can easily be answered by simply measuring the specific heats and deriving the entropy diagrams. As Fig. 17 shows, the two entropy diagrams for helium and for a superconductor are remarkably similar. There is a linear drop toward absolute zero in the normal state —in the metal before it becomes a superconductor, or in the helium I. This is followed by a much more rapid decrease in entropy as superfluidity sets in. It is tempting to connect this drop in entropy with the phenomenon of superfluidity; this can be done because superfluids seem to be mixtures of a curious kind. The so-called two-fluid model for superfluids has been used extensively, and in spite of certain shortcomings it is useful in explaining the properties. In this model the superfluid is considered as being made up of the same particles—that is, electrons diluted in electrons in the superconductor, and helium atoms diluted in helium atoms in the lambda phenomenon. As, on cooling, the transition temperature is passed, some of these particles pass into a state of lower energy, and finally, at 0 degrees Kelvin, the whole assembly is made up of these lower energy particles. So, as the temperature is decreased, the superfluid constituent in both cases increases all the time at the expense of the normal one. Such a mixture model will have exactly all the requisite properties. For instance, if one has an oscillating disk in helium, it will be impeded by the normal part of the fluid, but if one has a capillary, then the superfluid part will run through the capillary and give the impression of a much smaller viscosity.

As long as we just talk about the normal and the superfluid part without going into any atomistic explanation, the model is comparatively innocuous and we can use it as a working hypothesis. For instance, we can make experiments on the flow of the superfluid constituent, measuring its entropy separately. In a persistent current only the superconducting electrons take part in the motion, and in flow through a capillary only the superfluid part. By making a suitable type of measurement, we can determine the entropy of that part of the two-fluid model which moves without friction. It turns out that this entropy is zero in both cases. The drop in entropy (Fig. 17) is thus due to the growth of the superfluid

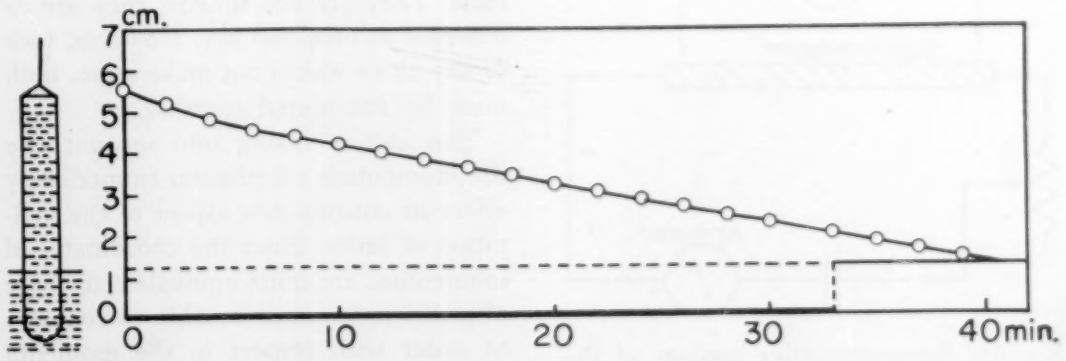

Fig. 14. Superflow takes place at a steady rate.

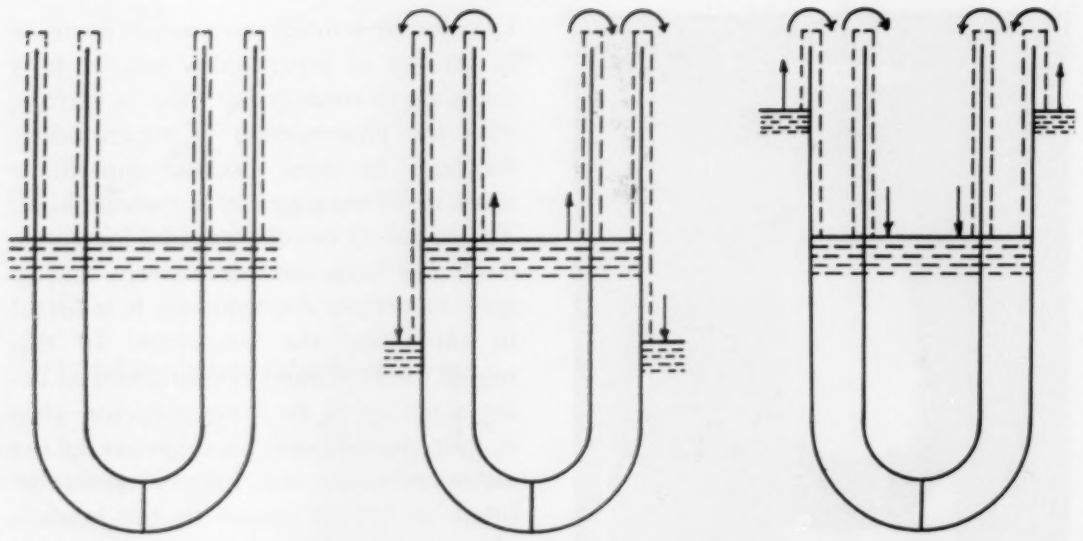

Fig. 15. Experimental demonstration of zero friction.

phase at the expense of the other phase, and to the fact that the superfluid phase has zero entropy. This constitutes no violation of the third law of thermodynamics for the simple reason that we cannot separate these two phases without a change in temperature.

Whereas we can determine the amount by which order is increased, the concept of entropy is unfortunately so general that we cannot say anything about the way in which this order is increased. In order to get some idea, we have to start thinking afresh about the basic principles of defining order. In both these cases—that of the free electrons and that of the helium atoms—we deal with fluids and not with solids. There is, therefore, no crystallization, and all the aspects which we normally connect with the concept of order are missing. Therefore we have to ask ourselves: What is actually the concept of order?

For instance, the chairs in a lecture room are arranged in a definite predetermined pattern, which we consider as order. It seems to us quite natural that order involves position. We feel

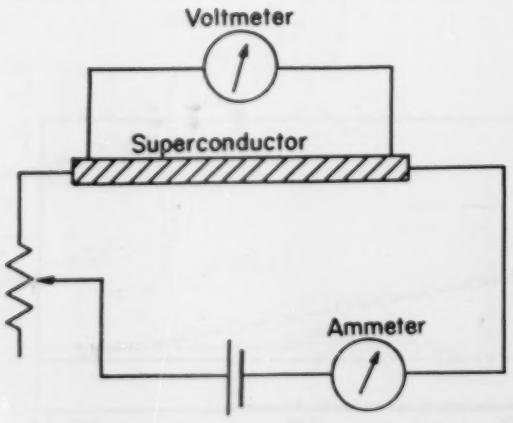

Fig. 16. Superconductive analogy of the double beaker experiment.

that we can only speak of order when we can talk about the relative position of one particle to another. But that is not quite true, because, as Gibbs showed long ago, in a description of a set of particles we do not deal only with the three dimensions of position-space; we must take into account all the six dimensions of phase-space—the three coordinates of position and the three coordinates of momentum.

Momentum and Position

The great strength of physics as a method is that it allows comparatively sure predictions. Modern technology is based on the combination of well-known principles, and these principles allow a fairly clear prediction of what will happen in the end. In order to make such a prediction, it is not sufficient to know the position of particles at one given time. We must also know their positions in the next instant. In other words, the momenta of the particles are as important as their positions. This complementarity is made clear by the fact that the uncertainty relation, the basic principle of quantum mechanics, does contain these two quantities, the position and the momentum, as complete equivalents. They are not similar; they are as different as lock and key. However, lock or key alone would not make sense; both must be considered together.

The idea of taking into account also the momentum coordinates immediately offers an entirely new aspect of the definition of order. Since the coordinates of momentum are quite equivalent to those of position, we must be able to conceive of order with respect to the momenta in the same way as we are accustomed to regard the chess-board pattern of position as a state of order. And it is perhaps significant that in the superfluids the striking features are provided by the transport phenomena. This means that the relevant phenomena are those which are connected with momentum, with the properties of motion, rather than with any static properties. The only difficulty appears to be that somehow our brains are so constructed that we cannot imagine happenings in momentum-space in the same way as we visualize happenings in position-space. On the other hand, if what we observe in the superfluids are momentum condensations, they do not occur in dimensions which are inaccessible to us. On the contrary, these are very striking phenomena which we can see. Perhaps we can make a model of velocity condensations conceivable even with our brains which are accustomed to position order.

In fact, a certain type of momentum condensation has been invented by all civilized governments—that is, those whose subjects own motors cars—by the introduction of a speed limit. Clearly if you have cars moving at all velocities from 5 to 100 miles per hour over the road and you then impose (and enforce) a speed limit of 30 miles per hour, then all the higher velocities will be compressed to 30 miles an hour. If you were to make a movie of this from a great

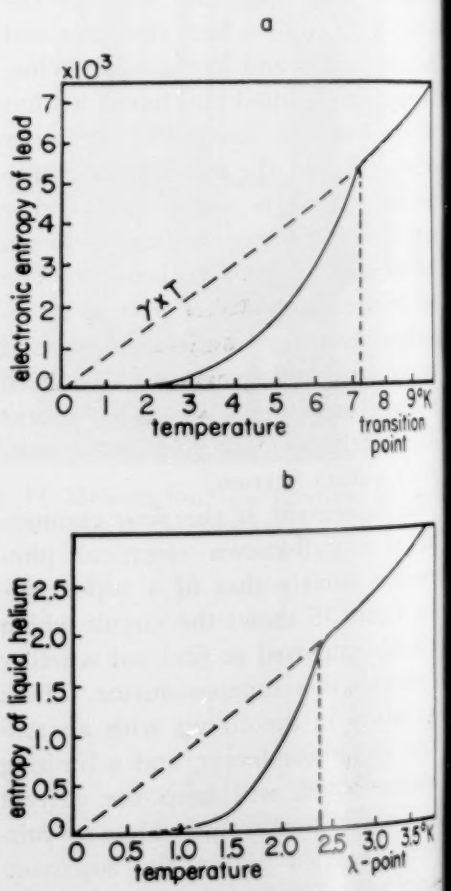

Fig. 17. Entropy diagrams of the electrons in a superconductive metal (*a*) and of liquid helium (*b*).

height, then although you would only observe positions at intervals, you would nevertheless see a pattern of order appear. Take a section of road somewhere where there are a bus, two cars, another bus, and a truck, and later look at the same string at quite a different part of the road. You will then note a degree of order if the relative positions of and distances between the vehicles have been maintained. This is clearly a condensation in momentum space. I would like to make it clear straight away that this model has no other merit than to show that we can understand, conceive, and recognize momentum condensations in our imagination, but this is certainly not the model which can be applied to liquid helium and superconductors. In our example, recognition of the pattern depends on our ability to make a distinction between the different vehicles, and of course one must not make a distinction between atoms. This is a classical model, and it shows nothing more than that momentum condensations can be created and might therefore possibly exist in nature.

Aggregation of Momenta

If we go that far and assume that momentum condensations are the basis of the phenomena of superfluidity, then we must immediately go one further step in our speculations. That is to assume that this order pattern must be of a very fundamental nature, because in the two cases which we know, electrons in superconductors and helium atoms in liquid helium, we deal with particles in very different settings and of a very different nature. In one case they are charged light particles in a metal matrix, which obey Fermi-Dirac statistics, and in the other case they are uncharged atoms which by themselves form a liquid and obey Bose-Einstein statistics. If the superfluid state occupies in momentum-space the same position as a crystal in coordinate space, then we can expect that, quite independently of the originating process, the model may be one of great generality. In the cohesion of a solid we may have exchange forces such as in a metal, or van der Waal's forces as in solid argon, or ionic forces as in sodium chloride. These are quite different processes, but they all result in a pattern with very much the same general properties—that is, they result in a crystal.

Last of all, one might ask whether helium and superconductivity are the only representatives of this new state of aggregation. We must call it a state of aggregation in the same way as we call a solid a state of aggregation, only here the aggregation is in momenta and not in positions. Probably on the crust of the earth, which is after all a very unrepresentative bit of the universe, these states may occur only in the laboratory. If, on the other hand, one considers the interior of astronomical bodies of not too high a temperature, it is quite conceivable that under those conditions of very high zero-point energy, the state of aggregation of this frictionless pattern may be more favored than that of position. In fact, we know that here position-order is quite impossible. It thus may turn out that the frictionless state of aggregation is the common form of aggregate matter in the universe, and that the solid state is a rather strange oddity reserved for our own odd corner of the universe.

That is one possibility, but there is another one. We can, of course, become bolder and, knowing the position condensates in the form of crystals, having postulated and almost believed in momentum condensates in the form of superfluids, we can look around in Gibbs space for further possibilities. There are regions in it where we must find other condensates, mixed condensates of position and momenta. We do not know what these mixed condensates can be, but we can say beforehand what properties they must have. They must have very low entropy, because you have here the chance of ordering to a very great extent. Second, they must have the properties of position-order—that is they must be tangible things with a given volume and shape. Third, they must have the characteristic properties of a condensation in momentum. One of the significant properties is that some essential feature is spread over the whole volume of the momentum condensate. Take, for instance, a superconducting ring. If there were no current in the ring and you cut it somewhere, not much harm would be done. There would be an array of atoms not much different from the atoms before cutting. It would not be generally noticed that the ring had been cut. But once a persistent current is flowing and you cut the ring, the whole current disappears from it. This means that the condensation or ordering in respect to the momentum vector, which you have destroyed locally, is now destroyed over the whole of the ring. Therefore, the properties of these velocity condensates are characteristic of the whole structure, and if you cut it in two, it has lost its meaning. If one tries to think where we might find structures like this, one sees that they are very improbable in the first place. They must have low entropy, they must be tangible structures, and they will lose their significance if they are cut in two. There are indeed structures which fulfill these conditions—the structures of living matter. However, this is just an amusing speculation.

Human Rhodopsin

George Wald and Paul K. Brown

The first measurement of the absorption spectrum of rhodopsin involved a human preparation (*1*). Arthur König had asked his colleagues Köttgen and Abelsdorff to measure the absorption spectrum of frog rhodopsin, hoping that the experience gained with this material might eventually be turned to the measurement of human rhodopsin. Before any frog pigment was measured, however, König unexpectedly received the gift of a single human eye. This was extracted with bile salts, and it yielded enough solution for three fillings of a microabsorption vessel. With the first filling König and Köttgen measured the absorption spectrum of human rhodopsin; with the second, the spectrum of a partly bleached solution. The third portion had begun to rot and was discarded.

König and Köttgen measured what we should now call the difference spectrum of rhodopsin—the difference in absorption spectrum before and after bleaching—in the mistaken belief that it was the true absorption spectrum. They found this to be maximal near 500 millimicrons (mμ). Assuming that the rhodopsin had been evenly spread over the rod-containing area of the retina, König computed that its absorption coefficient *in situ* was about 0.038 at 500 mμ, corresponding to an extinction of 0.0165.

König proceeded to compare this difference spectrum with the spectral sensitivity of human rod vision, measured in a totally color-blind subject and in the normal eye. Both sensitivity functions were corrected for the energy distribution of the source and for losses of light in the eye caused by absorption by the yellow lens and the pigment of the *macula lutea*. In this way König derived spectral sensitivity functions for rod vision, as though measured at the receptor layer. These functions corresponded closely with the difference spectrum of human rhodopsin. In this experiment, therefore, König and Köttgen provided the first direct demonstration that rhodopsin is a *visual* pigment and set the main themes for this type of investigation.

Recently Crescitelli and Dartnall (*2*) measured a second preparation of human rhodopsin, again obtained from a single retina. The difference spectrum at *p*H 8.2 was found to be maximal at 497 ± 2 mμ. The extinction of this pigment in the retina (assuming it to be evenly distributed over the rod surface) was estimated to be about 0.016, almost exactly König's result. The absorption spectrum inferred tentatively on the basis of these measurements was found to agree reasonably well with the spectral sensitivity of human rod vision, calculated on a quantum basis and corrected for the transmission of the ocular tissues. In accordance with a system of nomenclature proposed earlier by Dartnall, it was suggested that human rhodopsin be called "visual pigment 497."

Preparation

We have recently obtained a number of human eyes, within several hours following enucleation (*3*). No special precautions were taken to adapt them to the dark. The retinas were removed under dim red light and stored in the dark at −10°C until used. The retinal tissue was ground with a mortar and pestle in 40-percent sucrose solution, and the outer segments of the rods were separated from the remaining retinal tissues by differential centrifugation, as described earlier (*4*). The rods were washed free from sugar and buffer and were hardened by treatment with 4-percent alum solution for 15 minutes. They were washed once again with distilled water and neutral phosphate buffer, frozen-dried, and extracted with petroleum ether to remove fat-soluble material. The residue was then extracted with 2 percent digitonin in phosphate buffer at *p*H 6.5 to solubilize the rhodopsin and opsin.

Absorption Spectrum

The absorption spectrum of a solution of human rhodopsin is shown in Fig. 1. It displays the three usual absorption bands. The α-band, which dominates the visible spectrum, is maximal at 493 mμ. This is an extraordinarily short $\lambda_{max.}$, shorter than that of any vertebrate rhodopsin previously examined, with the exception of that of certain deep-sea fishes. Indeed, it corresponds in this regard to the rhodopsin of a marine fish living at a mean depth of about 60 fathoms (*5*). The spectrum continues with a minimum at about 390 mμ, a small β-band at about 350 mμ, and the tall γ or opsin band at 278 mμ. The ratio of extinctions at 390 and 493 mμ ($E_{min.}/E_{max.}$) is 0.24. We believe that this spectrum is virtually that of the pure pigment down to about 320 mμ. The γ-band probably involves, in part, other proteins. When this pigment is bleached in orange—nonisomerizing—light, the α- and β-bands are replaced by the absorption band of all-*trans* retinene, maximal at about 380 mμ.

Figure 2 shows the absorption spectrum of another such preparation of human rhodopsin, measured in the presence of 0.1*M* hydroxylamine (*6*). When this solution is bleached with orange light, the retinene reacts rapidly with hydroxylamine to form all-*trans* retinene oxime ($\lambda_{max.}$ 367 mμ). This possesses a molar extinction of 51,600 in digitonin solution. In several such experiments we have found the $E_{max.}$ of human rhodopsin to be 0.76 to 0.79 times as high as the $E_{max.}$ of the retinene oxime formed by its bleaching. Therefore, its molar extinction $\varepsilon_{max.}$ must be 0.76 to $0.79 \times 51{,}600$, or $40{,}000 \pm 800$—close to that of cattle rhodopsin (*6*).

The difference spectrum of human rhodopsin, bleached in the presence of hydroxylamine, is also shown in Fig. 2. Since the absorption of light by retinene oxime is negligible at wavelengths longer than 450 mμ, the difference spectrum is identical with the true absorption spectrum of rhodopsin above this wavelength. The hydroxylamine difference spectrum represents an absolute measurement, independent of the presence of colored impurities and invariant with *p*H. It offers the opportunity to obtain the absorption spectrum of pure rhodopsin above 450 mμ from preparations however impure. It shares an inter-

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esting empirical characteristic with cattle rhodopsin the change in extinction at the maximum almost exactly equals the change in extinction at the minimum ($\Delta E_{max.} = \Delta E_{min.}$).

Homogeneity

We have found that a useful characterization of both the shape and position of the rhodopsin spectrum is provided by the ratio of the extinction at 540 mμ to that at the maximum ($E_{540}/E_{max.}$) (*5*). For human rhodopsin this ratio is 0.436. (For a rhodopsin with $\lambda_{max.}$ 497 it would have been 0.55.) To test the homogeneity of the preparation from which Fig. 2 was derived, it was partly bleached, successively, with near-ultraviolet light containing wavelengths shorter than 400 mμ (Wratten 18A filter) and with orange light containing wavelengths longer than 550 mμ (Jena OG2 filter), all in the presence of hydroxylamine. The $\lambda_{max.}$ of the difference spectra for both types of bleach is about 493 mμ. The $E_{540}/E_{max.}$ ratios were essentially identical: 0.443 for bleaching in blue light and 0.436 for bleaching in orange light.

A further evidence of homogeneity is found in the spectra shown in Fig. 3. In this case a rhodopsin preparation was bleached in the deep orange of a Jena OG3 filter (wavelengths greater than 565 mμ). The sharp isosbestic point at about 432 mμ shows that a single photosensitive pigment bleached to a single light-absorbing product (all-*trans* retinene). The kinetics of bleaching follows the course of a first-order reaction, proportional in rate to the intensity of the light.

Composition and Regeneration

The bleaching of human rhodopsin in nonisomerizing light results in an inactive mixture of all-*trans* retinene and opsin. If neo-*b* (11-*cis*) retinene is incubated with this mixture in the dark, rhodopsin is regenerated (*7*). Human opsin has also been prepared from bleached retinas; it forms rhodopsin when it is incubated in the dark with neo-*b* retinene. All such preparations synthesized or regenerated *in vitro* have $\lambda_{max.}$ about 493 mμ and are indistinguishable from the rhodopsin extracted from human retinas (Fig. 4, right). It is clear that the exceptionally low $\lambda_{max.}$ of human rhodopsin derives from its peculiar opsin and not from an unusual prosthetic group.

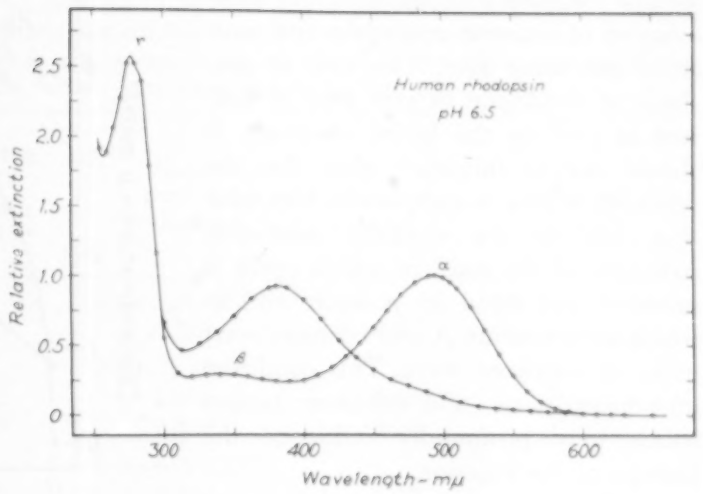

Fig. 1. Absorption spectra of human rhodopsin and the product of its bleaching in 2 percent aqueous digitonin solution. The α-band of rhodopsin has been set arbitrarily at $E_{max.} = 1$. On bleaching in orange (nonisomerizing) light, the α- and β-bands of rhodopsin are replaced by the absorption band of all-*trans* retinene ($\lambda_{max.}$ 380 mμ). The γ- or opsin band at 278 mμ remains unchanged.

The kinetics of regeneration of human rhodopsin in solution is shown in Fig. 4. The reaction mixture, containing 3.90 μmoles of opsin and 25.6 μmoles of neo-*b* retinene per liter, was incubated in the dark at *p*H 6.5 and 29.5°C. The synthesis of rhodopsin was complete in about 30 minutes and half-complete in about 2.5 minutes. As is usual, the regeneration follows the course of a second-order reaction The rate constant *k* equals 0.0084 liter per μmole minute, or 39 liters per mole second.

The regeneration of rhodopsin has recently been measured in the living human eye by Campbell and Rushton (*8*). It pursues much the same course as human rod dark adaptation, when the latter is plotted as change of log sensitivity with time. Both processes are nearly complete in 30 to 45 minutes and half complete in 4 to 8 minutes. The synthesis of rhodopsin shown in Fig. 4 is a much more rapid reaction; at human body temperature it would have been half completed in about 1 minute.

The synthesis of rhodopsin *in vivo* involves a chain of reactions in which the combination of neo-*b* retinene with opsin is only the last step.Earlier steps include the hydrolysis of vitamin A esters, the isomerization of all-*trans* vitamin A or retinene to the neo-*b* configuration, and the diffusion of vitamin A from the pigment epithelium into the rods; the subsequent oxidation of vitamin A to reti-

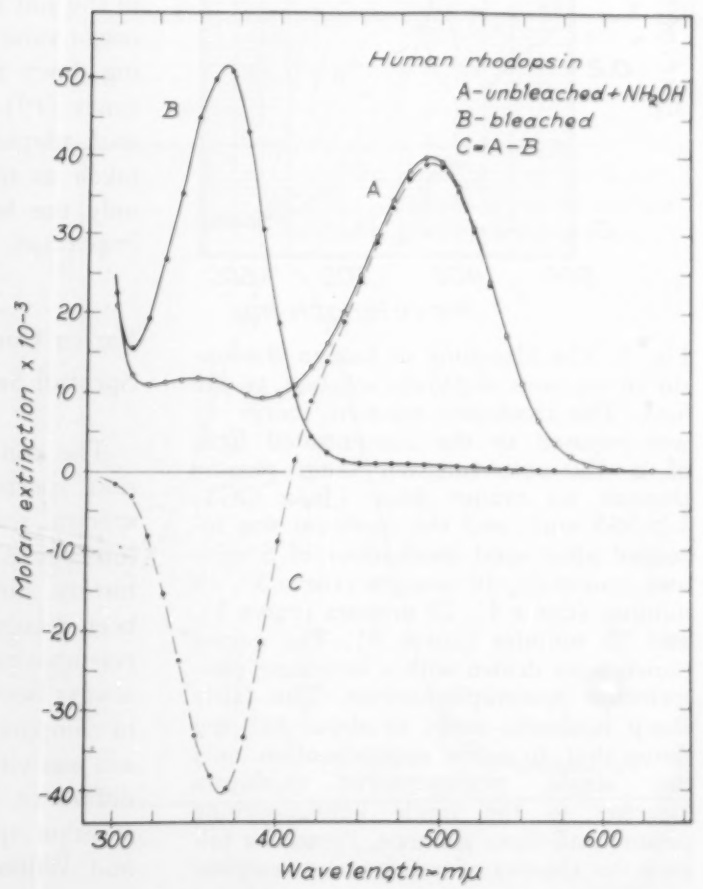

Fig. 2. Absorption spectra of human rhodopsin (curve *A*) and the product of its bleaching (curve *B*) in the presence of 0.1*M* hydroxylamine. Under these circumstances the product of bleaching is all-*trans* retinene oxime ($\lambda_{max.}$ 367 mμ). This compound does not absorb appreciably above 450 mμ; the small absorption of curve *B* above this wavelength is caused by a residue of unbleached rhodopsin. For this reason, also, the difference spectrum (curve *C*) is not quite identical with curve *A* above 450 mμ.

nene is coupled directly with the combination of retinene and opsin and must go at the same rate. The rate of synthesis of rhodopsin *in vivo* may be limited in part by the initial reactions. It should not be forgotten, also, that the synthesis *in vivo* occurs, not in free solution, but in the virtually solid-state structure of the rods, in which opsin is oriented and fixed in position and in which even vitamin A and retinene must move in restricted ways. This condition introduces steric and diffusion factors which may profoundly influence the kinetics of the reaction.

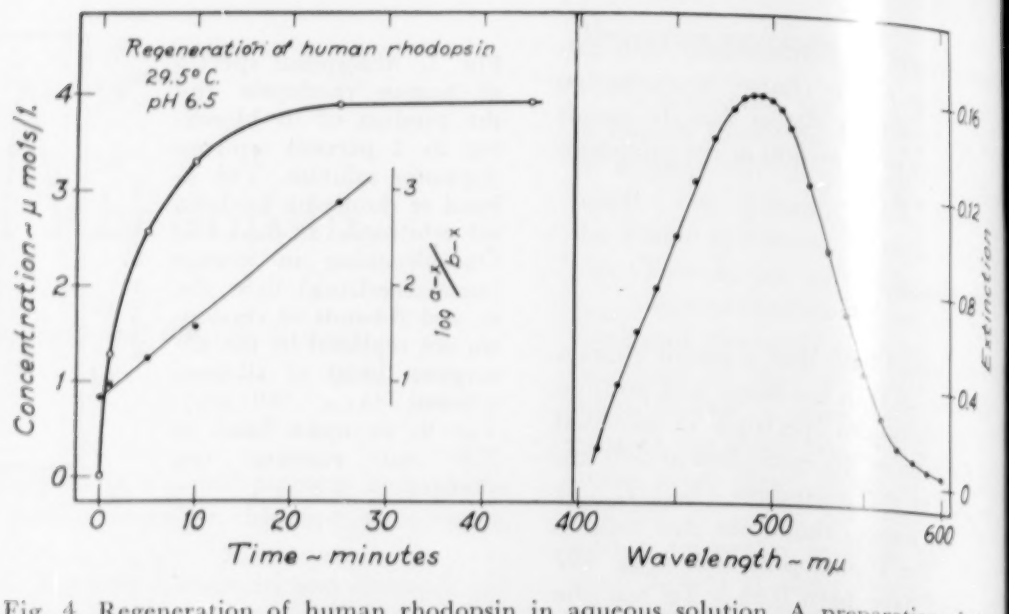

Fig. 4. Regeneration of human rhodopsin in aqueous solution. A preparation of rhodopsin was bleached in nonisomerizing light to an inactive mixture of all-*trans* retinene and opsin. This was incubated with neo-*b* retinene in the dark. The regeneration of rhodopsin followed the kinetics of a second-order reaction, as is shown by the linearity of the plot of log $[(a-x)/(b-x)]$ against time in the dark (a = initial concentration of neo-*b* retinene = 25.6 μmoles per liter; b = initial concentration of opsin = 3.90 μmoles per liter; x = concentration of rhodopsin at time t). At the right is shown the difference spectrum of the regenerated rhodopsin, measured in the presence of hydroxylamine. Its $\lambda_{max.}$ of 493 mμ is identical with that of the original pigment.

Concentration in the Retina

We have made preliminary attempts to measure the concentration of rhodopsin in the outer segments of the rods. Outer segments were isolated from the other retinal tissues by differential centrifugation and packed by centrifuging into the bottom of a hematocrit tube, and their volume was measured. They were then extracted, as has already been described. The measurements are summarized in Table 1. In four out of five determinations, performed with rods from three different groups of retinas, the values clustered about a mean extinction per rod of 0.015; in the fifth experiment the value obtained was 0.042. These values were computed on the assumption that the average length of the outer segment of a human rod in the parafoveal region is about 25 microns (*9*). No allowance was made for the orientation of rhodopsin molecules in the rod structure, which, if complete, might raise the extinction for light passing down the rod axis as much as 1.5 times (*10*). Since our retinas were not dark-adapted, these values should be taken as minimal. For this reason also only the highest value, 0.042, may be important.

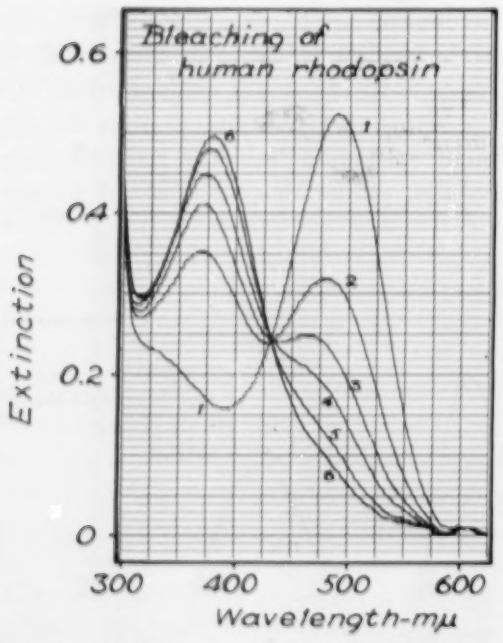

Fig. 3. The bleaching of human rhodopsin in aqueous digitonin solution at *p*H 6.45. The rhodopsin solution (curve 1) was exposed to the concentrated light of a 160-watt tungsten lamp passing through an orange filter (Jena OG3; $\lambda > 565$ mμ), and the spectrum was recorded after total irradiations of 5 minutes (curve 2), 10 minutes (curve 3), 15 minutes (curve 4), 25 minutes (curve 5), and 35 minutes (curve 6). The curves shown were drawn with a recording photoelectric spectrophotometer. The fairly sharp isosbestic point at about 432 mμ shows that, to a first approximation, only the single photopigment rhodopsin bleaches to the single light-absorbing product, all-*trans* retinene. Bleaching follows the kinetics of a first-order reaction.

Earlier Comparisons with Spectral Sensitivity

The comparison between the absorption spectrum of rhodopsin and the spectral sensitivity of human rod vision, introduced by König, has had a peculiar history. Since the time of König it has been recognized that these two functions resemble each other closely; yet there has always been some fault in the data used to compare them. König's own comparison was vitiated in part by the use of the difference spectrum instead of the absorption spectrum of rhodopsin. Hecht and Williams restated this comparison on the basis of their new measurements of the human scotopic sensitivity, which they had found to be maximal at about 511 mμ. Again they employed the difference spectrum of rhodopsin [monkey and rabbit (*11*)], believing it to represent the absorption spectrum. They also omitted König's corrections for ocular transmission. The difference spectrum was maximal at about 503 mμ—that is, it was about 8 mμ shorter in wavelength than the visual sensitivity. Hecht and Williams suggested that this shift is caused by the fact that since the outer segments of the rods have a higher refractive index than aqueous solutions, rhodopsin in the former medium exhibits a shift of absorption toward the red in accordance with Kundt's rule (*12*).

The later development of this comparison succeeded in disposing of this difference in position between the rhodopsin absorption spectrum and spectral sensitivity, and hence of the necessity to invoke Kundt's rule. The data on spectral sensitivity were quantized (*13*) and were recorrected for ocular transmission (*14*), both operations shifting the curve toward shorter wavelengths. In place of the difference spectrum of rhodopsin employed earlier, a genuine absorption spectrum was substituted, and this was recomputed to correspond with estimates of the actual absorption of rhodopsin in the retina (*15*). When all these adjustments had been made, the spectral sensitivity computed as though at

the inner retinal surface agreed very well with the absorption spectrum of rhodopsin (*15*).

Such comparisons, however, involved until lately the rhodopsins of animals other than man: frog rhodopsin, with $\lambda_{max.}$ 502 mμ, or cattle rhodopsin, with $\lambda_{max.}$ 498 mμ. Crescitelli and Dartnall reintroduced an estimated spectrum of human rhodopsin, with $\lambda_{max.}$ 497 mμ; this agreed reasonably well with Crawford's (*18*) recent measurements of the scotopic sensitivity function.

The present measurements show, however, that the $\lambda_{max.}$ of human rhodopsin is at 493 mμ and that the entire absorption spectrum lies at distinctly shorter wavelengths than does the human scotopic sensitivity, however corrected. We are forced, therefore, to consider again Hecht's suggestion that, in the outer segments of the rods, the absorption spectrum of rhodopsin is shifted toward the red from the absorption spectrum in aqueous solution.

Absorption of Rhodopsin in Rods

To examine this possibility, we have measured the absorption spectrum of rhodopsin in suspensions of human rod particles. The particles from a fresh retina were separated from the remaining retinal tissues by differential centrifugation in 40 percent sucrose, as already described, and were examined without further treatment. The difference spectrum of such a suspension, measured in the presence of hydroxylamine, is compared in Fig. 5 with the difference spectrum of human rhodopsin in aqueous solution. Such data obtained with rod particles satisfy all the criteria of good difference spectra: for example, $\Delta E_{max.}$ almost exactly equals $\Delta E_{min.}$ However, $\lambda_{max.}$ lies at 500 mμ, shifted 7 mμ toward the red as compared with $\lambda_{max.}$ of the solution. The α-band of rhodopsin in the rod particles is also slightly *narrower* than it is in solution. Indeed, the spectrum in the rod particles exhibits much the same changes as are displayed by rhodopsin when it is measured at low temperatures in a rigid medium (*17*).

We have also recently measured directly the difference spectrum of the human retina. A portion of human retina, laid flat upon a microscope slide and backed with finely ground Vycor glass to diffuse the light, was measured against an identical microscope slide and ground glass as blank. Then the retina was bleached in position, and its

Table 1. Concentration and extinction of rhodopsin in outer segments of human rods. The average length of the outer segment of the rod in the parafoveal region is taken as 25 microns. No allowance is made for orientation of rhodopsin molecules in the rods, which may raise the extinction *in situ* as much as 1.5 times, or for other aspects of the solid state structure of the rods, which may raise the extinction still further.

No. of retinas	Volume of outer segments of rods (mm^3)	Volume of extract (ml)	$E_{max.}$ per cm (solution)	$E_{max.}$ per cm (rods)	$E_{max.}$ per rod (25 μ)
			1 February 1957		
3	11	0.5	0.367	16.7	0.042
			24 July 1957		
2	75	0.5	0.875	5.83	0.015
1	47	0.5	0.319	3.39	0.0085
			15 August 1957		
2	23	0.5	0.257	5.59	0.014
2	20	0.5	0.312	7.80	0.020

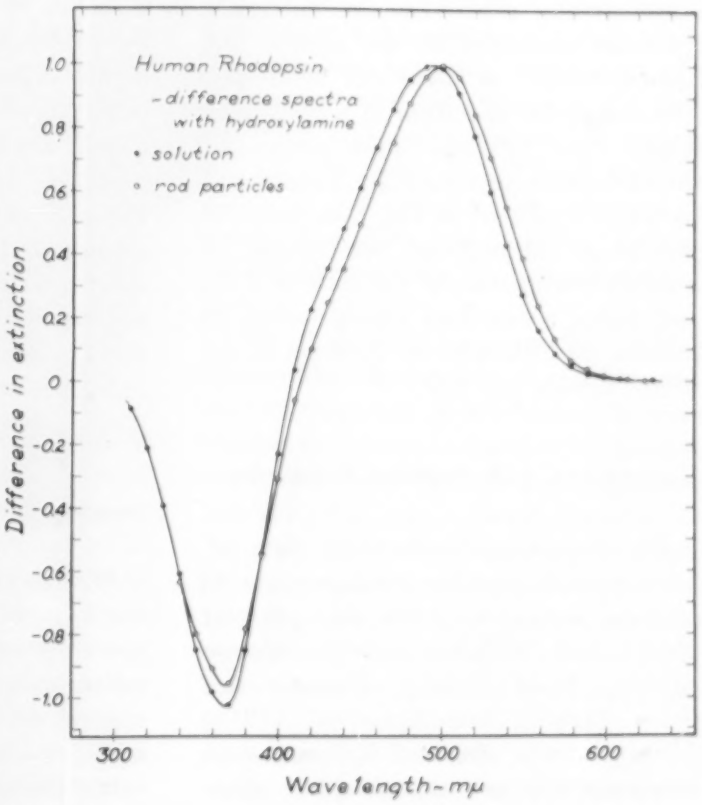

Fig. 5. Difference spectra of human rhodopsin in aqueous solution and in rod particles, measured in the presence of hydroxylamine. The $\lambda_{max.}$ in solution is 493 mμ; in a suspension of rod particles oriented at random it is 500 mμ. The spectrum in the particles is also narrower than it is in solution. At wavelengths longer than 450 mμ these difference spectra are identical with the absorption spectra.

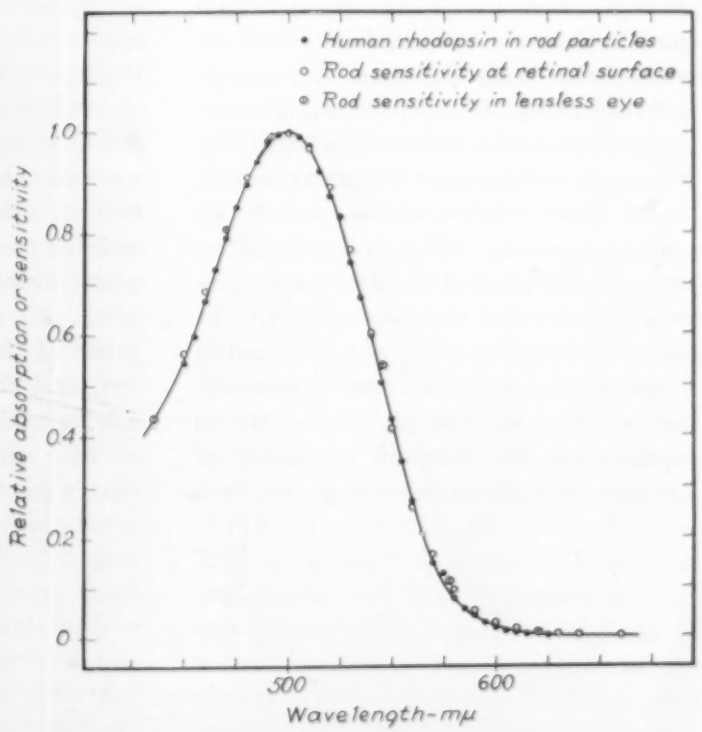

Fig. 6. Human rhodopsin and the spectral sensitivity of rod vision. The absorption spectrum of rhodopsin, measured in human rod particles, is compared with the scotopic (rod) luminosity function, quantized and corrected for ocular transmission so as to represent the sensitivity at the retinal surface, and with the scotopic luminosity (quantized) of the lensless human eye. In the latter, the principal colored structure of the eye, the yellow lens, having been removed in the operation for cataract, the luminosity function comes as close to the intrinsic sensitivity of the rods as one can approach *in vivo*.

spectrum was remeasured. The difference spectrum ($\lambda_{max.}$ 502.5 mμ), as expected, was displaced slightly from the hydroxylamine difference spectrum, owing to the fact that, in the absence of hydroxylamine, retinene itself absorbs light in the region of the rhodopsin maximum. The change in extinction at 502.5 mμ was 0.067. This must be taken as a minimal value, since the retina was not dark-adapted and since no allowance was made for the passage of light through spaces between the rods. It corresponds almost exactly with the highest extinction we have measured in unoriented rod particles (0.042; Table 1) multiplied by the orientation factor 1.5 (see *10*).

As already explained, the difference spectrum measured in the presence of hydroxylamine is identical with the true absorption spectrum at wavelengths longer than 450 mμ. This portion of the difference spectrum for human rod particles is plotted in Fig. 6 in terms of percentage absorption; we assume a maximal extinction in the rods of 0.15, and hence a maximal absorption of 29 percent, as estimated by Rushton in the living human eye (*18*).

Comparison with Spectral Sensitivity

For comparison with these data we have plotted together measurements of scotopic sensitivity from five sources: Hecht and Williams (1922), Weaver (1937), Wald (1945), Flamant and Stiles (1948), and Crawford (1949) (*19*). Between 450 and 650 mμ, these measurements are in very good agreement, and a freehand curve was drawn through them. This curve was then quantized and corrected for ocular transmission with the data of Ludvigh and McCarthy (*14*). The resulting measurements, which represent the sensitivity of human rod vision as though measured at the inner retinal surface, are shown with open circles in Fig. 6. In this figure we have also plotted the direct measurements of human scotopic sensitivity in an extramacular area of the lensless ("aphakic") eye (*20*). Such measurements come as close as is possible to representing the intrinsic sensitivity of the human rods in the living eye. It is clear that all these data agree very well with one another. There is enough leeway in present measurements of the human scotopic sensitivity function, and in the correction for ocular transmission, to permit as much closer a fit to the absorption data as one takes the trouble to obtain; but this would be gilding the lily.

We can conclude that, when adequately measured, the absorption spectrum of human rhodopsin and the spectral sensitivity of human rod vision correspond exactly. It is now clear, however, that this correspondence hangs upon a peculiar phenomenon: the displacement of the absorption spectrum of rhodopsin toward the red in the outer segments of the rods, as compared with the spectrum in aqueous solution. In the highly organized microstructure of the outer segments, the molecules of rhodopsin are fixed in position and highly oriented. In this regard, rhodopsin is virtually in the solid state. In consequence of this condition, its absorption spectrum is displaced toward the red and is narrower than in solution. It also presents a higher extinction for light passing down the rod axis, the normal direction of incidence *in vivo*.

Summary

Human rhodopsin in aqueous solution has $\lambda_{max.}$ of 493 mμ and is lower in the spectrum than the rhodopsins of all other known vertebrates, with the exception of certain deep-sea fishes. Its molar extinction is 40,000 ± 800. Like other rhodopsins, it bleaches to a mixture of opsin and all-*trans* retinene and is resynthesized by incubating opsin with neo-*b* (11-*cis*) retinene. The regenerated rhodopsin has the same $\lambda_{max.}$ as the extracted pigment; this is due, therefore, not to an unusual retinene but to a characteristic human opsin. The regeneration in solution from opsin and neo-*b* retinene is a second-order reaction with a half-time, at 29.5°C, of about 2.5 minutes. This is much faster than the synthesis of rhodopsin in the living human eye, and faster than human rod dark-adaptation; the rate of both processes *in vivo* must be limited by reactions which precede the union of neo-*b* retinene with opsin, the final step in rhodopsin synthesis. In the rods, rhodopsin is virtually in the solid state—highly oriented in close relation with other highly oriented molecules. In this situation its spectrum is displaced toward the red ($\lambda_{max.}$ 500 mμ) and is narrower than in solution. For light entering the rods axially, rhodopsin has also a considerably increased extinction, some 1.5 times higher than when randomly oriented. The spectrum of rhodopsin in rods agrees well in form and position with the spectral sensitivity of human rod vision, measured at the retinal surface.

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Samuel Randall Detwiler, Neuroembryologist

Samuel Randall Detwiler died suddenly in his office on the afternoon of 2 May 1957, in his 67th year, in an environment where he had spent the last 30 years of his distinguished career as professor and executive officer of the department of anatomy, College of Physicians and Surgeons, Columbia University. On 14 May his close friend and colleague, W. M. Copenhaver, paid a tribute to his memory at a memorial service held in the Pauline A. Hartford Chapel, Presbyterian Hospital, New York City. A Samuel Randall Detwiler scholarship gift has now been established at the College of Physicians and Surgeons, Columbia University, to perpetuate his memory.

Dr. Detwiler was born in Ironbridge, Pennsylvania, on 17 February 1890. After finishing preliminary school at an early age, he taught for a year in an old red country schoolhouse in Lancaster County, not far from his father's farm on which he had spent his youth. It was here that his early enthusiasm for teaching was aroused when, on the second day, he gave a thorough thrashing to the school bully and thus provided the atmosphere for a successful year in dealing with the three R's.

While still pursuing heavy duties on the farm, he attended nearby Ursinus College for two years. Then he transferred to Yale, where he obtained a B.S. degree in 1914. Here he came in contact with the distinguished embryologist Ross Granville Harrison, who very early directed his fertile mind into fields of research that later gained him a world-wide reputation as a neuroembryologist.

His doctoral thesis under Harrison dealt with experimental studies on the development of the anterior limb of the salamander, *Amblystoma punctatum*, in which he introduced the use of a vital dye, Nile blue sulfate, that soon became widely employed by experimental embryologists. Since it was always characteristic of Detwiler to have many successful research projects in progress simultaneously to satisfy his inquisitive mind, it is not surprising to learn that, while he was working on his doctoral thesis, he published two papers on the effects of light on the retina of reptiles. He retained an interest in this field over a long period, and at various times in subsequent years, on down to the time of his death, he published 34 papers on the retinae of all classes of vertebrates, studying particularly the structure of the rods and cones in nocturnal and diurnal animals, pigment migration in light and dark adaptations, photochemical responses, and induction of the neural retina from embryonic retina pigment cells. He epitomized his studies in 1943 in a monograph entitled *Vertebrate Photoreceptors*.

Early in his career Detwiler gained wide experience through working with distinguished scholars. At the time he received his Ph.D. degree from Yale, in 1918, he was also engaged in research on gas warfare with the well-known physiologist Yandell Henderson. Later, while on sabbatical leave in 1927, he worked with Hans Spemann in Freiburg, Germany. He gained wide experience as a teacher in several institutions. After two years as instructor in anatomy at the Yale University School of Medicine, he became a member of the faculty of the Peking Union Medical College, where he remained for three years. In 1923 he returned to the States as associate professor in zoology at Harvard—a position which he held until 1927, when he was called to Columbia University to accept the chair in anatomy previously held by Huntington. Here he built up one of the largest departments of anatomy in this country and in many ways played an important role in the development of the Columbia-Presbyterian Medical Center.

The largest portion of Detwiler's publications lies in the field of neuroembryology. Many of his 155 published papers and one book, *Neuroembryology*, dealt with the developing urodele limb bud, in connection with which he devised numerous clever experiments to show the guiding influence that the end organ exerted upon outgrowing spinal nerve fibers as the limb was shifted to new positions along the spinal cord. The normal nerves of the brachial plexus were eliminated, one by one, by the conditions of these experiments, and other spinal nerves took their places. Through his studies of coordinated limb movements he found that there was a central limb-coordinating mechanism. Among his many studies of the development of coordinated movements in salamander larvae he included studies of the role of the Mauthner's cell in the medulla and revealed its relation to sustained swimming movements.

He performed many experiments to show that hypoplasia of the sensory elements in the spinal cord and ganglia took place in the absence of a limb, while hyperplasia occurred in the presence of a peripheral overload created in the limb area. He also exchanged various regions of the embryonic spinal cord and the medulla and revealed the influence of developing fiber tracts upon cellular proliferation within the central nervous system.

His ingenious experiments, which showed that the number of spinal ganglia and the number of spinal nerves were dependent upon the number of somites, are classic examples of an imaginative solution of a long debated question. In fact, the role and influence of the mesodermal somites in development was the subject of his last investigation, made in collaboration with Mrs. R. H. Van Dyke with whom he had published many papers in recent years. This paper came to press after his death.

Detwiler's numerous scientific achievements brought him many honors. Yale awarded him an honorary degree in 1931. In 1954–1955 he was president of the American Association of Anatomists. He was also a member of the editorial boards of the *Journal of Experimental Zoology*, *Experimental Biology* (Monograph Series), and the Columbia Biology Series.

"Det," as he was known to his numerous friends, was endowed with many talents. He possessed a warm, friendly personality and a great sense of humor. His success as a lecturer and teacher is well known by all who came in contact with him, for he threw the same intense energy and drive into these undertakings that he brought to all his other activities. He was a gifted musician. His students and friends will long remember his fine tenor voice as he joined or led them in song. His talents as a sculptor are revealed in the numerous portrait busts he made of many of his colleagues. He also

created over a hundred fine wood carvings.

His enthusiasm for creative work continued during his summer vacations, which were spent on his farm in New Hampshire among several of his lifelong friends. Here he built a laboratory for his scientific work and a studio where he spent many hours enjoying the pursuit of art with his wife Gladys, who is a talented painter and etcher. The farm played a major role in his life, and it will always be a reminder to his friends of the happy summer days in the place Det loved so well.

LEON S. STONE
Yale University School of Medicine, New Haven, Connecticut

News of Science

College Enrollments in 1957

College enrollments set a new record in 1957 for the sixth year in a row and will climb substantially with the opening of the second semester, according to the U.S. Office of Education in its January issue of *Higher Education*. A total of 3,068,000 students enrolled in 1890 colleges and universities early last fall, an increase of 4.1 percent over the 2,947,000 who enrolled in the fall of 1956.

Last fall's enrollment was 45 percent above fall enrollments in 1951, the year of lowest enrollments since World War II, and 25 percent above 1949, the peak year for enrollments in the immediate post-war years. During the remainder of the school year, college and university enrollments are expected to climb to an all-time high of approximately 3,460,000. The 45-percent increase in college enrollments since 1951 compares with an increase of only about 2 percent during the same period in the number of persons 18 to 21 years of age. Nearly two-thirds of the 1957 college student body —2,003,000 of the total 3,068,000—are men.

Because of an unprecedented increase in the number of births during the mid-1940's, the number of college-age persons in the population will start to climb steeply in the early 1960's. In the next decade, the number of young people seeking enrollment in college is expected to double. Despite the larger proportion of young people going to college in recent years, there are still large numbers of able students who do not obtain a college education.

The ten institutions which led in the number of students this year are as follows: University of California (all campuses), 41,598; University of Minnesota (all campuses), 35,852; New York University, 31,068; State University of New York (all campuses except the Agricultural and Technical Institutes), 29,883; City College of the City of New York, 28,181; Columbia University, 26,787; University of Michigan, 26,370; University of Illinois, 25,920; University of Wisconsin (all campuses), 24,873; and Ohio State University, 22,611.

Total opening enrollment in liberal arts colleges increased 6.5 percent over 1956; in junior colleges, 6.2 percent; in teachers' colleges, 6 percent; in technological schools, 3.4 percent; in separately organized professional schools (other than teachers' colleges and technological schools), 3.3 percent; in universities, 2 percent; and in theological and religious schools, 1 percent.

The greatest increase in first-time students last fall occurred in other separately organized professional schools, in which enrollment increased 9 percent over 1956. Increases also were reported for teachers' colleges (4.4 percent), junior colleges (2.9 percent), theological and religious schools (2.5 percent), and liberal arts colleges (2.4 percent). Decreases were reported by universities (2.9 percent), and technological schools (0.6 percent).

Publicly controlled institutions reported a 5.9 percent gain in number of students over the fall of 1956, while privately controlled institutions listed 1.8 percent more than last year. First-time enrollment in both types of schools increased 0.9 percent. Of the total college population, 58 percent were attending publicly controlled institutions in 1957 and 57.1 percent in 1956.

States with increases of 10 percent or more included Delaware (14.4 percent, including enrollment in a newly reclassified institution not counted in 1956 enrollments), Virginia (13.9 percent), Maine (12.8 percent), Arkansas (11.7 percent), and New Mexico (10 percent). Fewer college students were reported in three states. The largest decrease was in Nevada (5.2 percent).

Delaware—the reclassified institution mentioned above was again a factor—reported a 47.2 percent increase in first-time enrollment. Also reporting a gain of 10 percent or more were Arizona (24 percent), Oregon (14.2 percent), Maine and Massachusetts (12.1 percent each), and New Jersey (11.1 percent).

The number of students attending college for the first time declined in 17 states and in the service academies. Decreases of 5 percent or more were reported in South Dakota (9.7 percent), Indiana (8.2 percent), Ohio (7.8 percent), Virginia (7.4 percent), Utah (7 percent), Georgia (6.2 percent), Oklahoma (5.3 percent), and New Hampshire (5 percent), the U.S. service academies (15.9 percent).

Fellowships in Science Journalism

An advanced Science Writing Program, financed by a pilot grant of $70,000 from the Alfred P. Sloan Foundation, is being established at Columbia University's Graduate School of Journalism. Promising young reporters and writers will be invited to spend an academic year at the university on fellowships that cover their class, tutorial, and seminar costs, plus approximately $550 a month for living expenses. Most recipients will have scientific interests as well as three to six years of experience on newspapers, magazines, wire services, radio, or television. The program will draw upon specialists from the other faculties of Columbia University and will be kept flexible to meet individual interests.

Commenting on the grant, Edward W. Barrett, dean of the Graduate School of Journalism, said: "While only four to five full fellowships a year can be financed under the initial grant, it is hoped soon to expand the program to provide for ten fellows a year. The school also hopes later to experiment with writing courses for selected young scientists and to initiate short-term conferences for established science writers."

Dean Barrett also listed five important needs that the advanced Science Writing Program should help meet:

"First, to increase the number of dependable science and technology writers on newspapers, press services, magazines, radio and television and industry;

"Second, to increase substantially the number of reporters and editors who, though not devoting full time to science, will be able to handle such material interestingly and accurately;

"Third, to provide a means of helping present science writers to broaden their knowledge of both subject matter and techniques;

"Fourth, to provide a modest number of individuals capable of giving science-writing instruction at other institutions, and;

"Fifth, to serve as a pilot project whose experience can be drawn upon by other institutions."

Court Voids 18-Month Limit on Dismissal Suits

A Government rule barring reinstatement to Civil Service of people who waited more than 18 months to challenge their dismissals for alleged security reasons has been struck down by the U.S. Court of Appeals in Washington. The court, in a 2-to-1 decision on 1 January, held the 18-month limit unreasonable. The decision may open the way for a number of former Government employees to sue for reinstatement and back pay.

The Justice Department established the 18-month rule after the decision of the Supreme Court in the case of Cole v. Young. The decision, handed down on 11 June 1956, was that the Government could dismiss as security risks only employees in sensitive positions. During the three previous years many persons in non-sensitive positions had been dismissed under the Eisenhower security program. The decision in Cole v. Young meant that their dismissals had been illegal.

Marine Microbiology Laboratory

The Institute of Marine Science of the University of Texas has recently established a marine microbiology section under the direction of Carl H. Oppenheimer. The institute is situated on Mustang Island at Port Aransas, approximately 25 miles north of Corpus Christi. The laboratory provides facilities for studying the relationships of bacteria to the many environments nearby. Close at hand are attached algal flats, muddy bottom bays, accumulations of organic matter, oyster reefs, continental shelf environments, rock jetties, open beaches, and various sources of pollution. A course in marine microbial ecology will be offered during the summer. A curriculum has been established for advanced degrees with emphasis on marine bacteriology through the department of bacteriology of the University of Texas.

Grants, Fellowships, and Awards

Chemistry. The Division of History of Chemistry of the American Chemical Society is soliciting nominations for its $500 Dexter Award. The award is made on the basis of services that have advanced the history of chemistry in any of the following ways: by publication of an important book or article; by the furtherance of the teaching of the history of chemistry; by significant contributions to the bibliography of the history of chemistry; or by meritorious services over a long period of time which have resulted in the advancement of the history of chemistry. All information, in duplicate, should be sent before 10 March to the secretary of the division, Sidney M. Edelstein, Dexter Chemical Corporation, 819 Edgewater Rd., Bronx 59, N.Y.

Ophthalmology. The National Institute of Neurological Diseases and Blindness has announced the establishment of a special travel fund to aid younger ophthalmologists and other scientists engaged in ophthalmological teaching or research to attend the 18th International Ophthalmology Congress that is to be held in Brussels, Belgium, 8–12 September. The fund was made possible by a grant from the National Advisory Neurological Diseases and Blindness Council to a Council subcommittee. All applications for aid from the fund should be submitted before 1 March to Dr. Gordon H. Seger, Chief, Extramural Programs, National Institute of Neurological Diseases and Blindness, Bethesda, Md.

Psychiatry. The Foundations' Fund for Research in Psychiatry has announced the availability of a limited number of block grants (fluid funds) for research in departments of psychiatry in medical schools and clinical facilities with established training programs. Applications should be submitted before 1 March. For further information, department representatives are invited to write to the Executive Officer, Foundations' Fund for Research in Psychiatry, 251 Edwards St., New Haven 11, Conn.

Sex. The Division of Medical Sciences of the National Academy of Sciences–National Research Council is accepting applications for grants-in-aid of research for consideration by the Committee for Research in Problems of Sex. The funds for support of this program are provided by the Rockefeller and Ford foundations. The committee is concerned primarily with encouraging research on the mechanisms underlying sexual behavior, with special emphasis on the higher mammals and man. Proposals involving endocrinological, neurological, psychological, anthropological, phylogenetic, and genetic studies directed toward this objective are therefore invited. Requests that deal with the physiology of reproduction or with related biological and biochemical fields should be addressed to the committee only if they give promise of shedding light on behavioral mechanisms.

Preliminary inquiries should be addressed to Room 309, Division of Medical Sciences, National Research Council, 2101 Constitution Ave., NW, Washington 25, D.C. Completed applications for the fiscal year 1958–59 should be postmarked on or before 7 March.

News Briefs

Award of 59 unclassified physical research contracts with universities and private research institutions has been announced by the U.S. Atomic Energy Commission. Six are new contracts, and the remainder are renewals of contracts which have been in force.

* * *

It is possible to transplant a tooth from one part of a patient's mouth to another in carefully selected cases. Chester C. Fong and R. Gordon Agnew, both oral pathologists of the College of Dentistry, University of California, describe a technique for surgically transplanting the third molar in an early stage of root development to the site of a missing permanent first molar in the January issue of the *Journal of the American Dental Association.*

* * *

Frank Pace, Jr., president of the International Golf Association, has announced that the proceeds of $10,000 from the fifth International Golf Championship and Canada Cup Matches, held this year in Tokyo, Japan, will be set aside to establish a scholarship fund for Japanese students to study nuclear science at American universities. The establishment of this scholarship fund was the result of an agreement between Pace and Matsutaro Shoriki, owner and president of the Yomiuri Shimbun newspapers, which cosponsored the event with the Japan Golf Association.

* * *

University of Cincinnati excavations in Greece at the site of King Nestor's palace have brought to light a beehive tomb from an earlier generation—probably that of King Neleus, Nestor's father—and a hitherto unknown northeast wing of the palace. These are among the major discoveries in the sixth year of the university's archeological investigations

at Nestor's 3000-year-old palace. Carl W. Blegen, professor emeritus of classical archeology, directs the annual excavations near the Greek seaport town of Pylos.

* * *

The Robert A. Welch Foundation, Houston, Tex., reports that its trustees have approved the renewal of 28 grants and the establishment of four new grants to support fundamental chemical research at nine institutions within the state of Texas. These 32 grants amount to a total of $1,066,993.

Scientists in the News

DETLEV W. BRONK, president of the National Academy of Sciences and president of the Rockefeller Institute for Medical Research, has received the gold medal of the International Benjamin Franklin Society.

GEORGE W. HERVEY, one of the founders of the post-war Red Cross Blood Program and its director of statistics since it was established 10 years ago, retired on 31 December from Red Cross service. He was appointed on 1 September 1947, becoming one of a small staff chosen to plan and launch the now nation-wide program. The first of the 51 Red Cross regional blood centers was opened in Rochester, N.Y., on 12 January 1948. Hervey developed methods of collecting and analyzing scientific and operational data that contributed greatly to the success of the program.

In 1957, Hervey acted as consultant to the Joint Blood Council in conducting a national survey of blood usage and collection facilities. The council is composed of the Red Cross, the American Association of Blood Banks, the American Hospital Association, the American Medical Association, and the American Society of Clinical Pathologists.

Now a colonel (retired) in the Medical Service Corps, U.S. Army Reserve, Hervey, as an Army officer in World War II, conducted manpower surveys at installations throughout the United States. He was awarded the Army commendation ribbon and later received the War Department's civilian certificate of appreciation for special studies of Army general hospitals.

Hervey received his bachelor of science degree from Rutgers University in 1915, his master of science degree from the University of Missouri in 1920, and his doctor of science degree from Harvard University in 1927. He now lives in Arlington, Va.

Recently the Royal Society (London) had its 295th anniversary. As is customary at the annual birthday celebration, society medals were presented.

Sir HOWARD FLOREY, professor of pathology at the University of Oxford, received the Copley Medal, senior award of more than £1000. Florey is best known for his work on penicillin. He is still working on antibotics, particularly in connection with treatments for tuberculosis.

The society's two Royal Medals—one for the physical science, one for the biological—went to W. V. D. HODGE, Cambridge mathematician and creator of the theory of harmonic integrals, and F. G. GREGORY, the plant physiologist who is probably best known for his work on the mechanism which brings about flowering and the reproductive phase in plants.

Dame KATHLEEN LONSDALE received the Davy Medal for her work on crystal chemistry. The medal is given annually for the most important discovery in chemistry made in Europe or North America.

Other medalists were Sir NEIL HAMILTON FAIRLEY, who received the Buchanan Medal for his research on tropical medicine, and J. PROUDMAN, who was awarded the Hughes Medal for his outstanding work on dynamic oceanography, and in particular on storm surges.

RICHARD COURANT, director of New York University's Institute of Mathematical Sciences, was honored at a convocation on 8 January to celebrate his 70th birthday. Courant has been head of the department of mathematics at N.Y.U.'s Graduate School of Arts and Science since 1934 and scientific director of the Institute of Mathematical Sciences since its creation in 1953. Before joining N.Y.U. he was professor of mathematics and director of the Mathematics Institute at the University of Göttingen, Germany.

FRANK BRINK, JR., has been appointed to the newly created office of dean of graduate studies at the Rockefeller Institute. Brink is a member and professor of the institute who is conducting research in biophysics. As dean, he will assist the president and the faculty committee on educational policies in the development of graduate education. He will organize the programs of lectures, seminars, and laboratory instruction and will counsel with graduate students and their faculty advisers.

There are nine scientists among the ten young men under 35 years of age selected by the United States Junior Chamber of Commerce as Outstanding Young Men of America for 1957. They are: THOMAS G. BAFFES, Skokie, Ill., surgeon, developer of a surgical correction for transposition of the great vessels of the heart; WILBERT E. CHOPE, Columbus, Ohio, president and founder of Industrial Nucleonics Corporation; RICHARD A. DEWALL, Minneapolis, Minn., surgeon, developer of a simplified mechanical heart-lung machine; ALFRED J. EGGERS, JR., Los Altos, Calif., aeronautical research scientist in the area of small-scale models for missile testing; DWIGHT D. GUILFOIL, JR., Arlington Heights, Ill., president and general manager of Paraplegics Manufacturing Company; KEITH E. JENSEN, Montgomery, Ala., medical microbiologist who is studying influenza viruses; ROBERT E. L. NESBITT, JR., Albany, N.Y., researcher in the cause and prevention of infant death in association with the birth process; MJ. DAVID G. SIMONS, U.S. Air Force, Holloman Air Force Base, N.M., physician-scientist who broke existing records for free-balloon flight exceeding 100,000 feet; CHEN NING YANG, Princeton, N.J., physicist, 1957 recipient of the Nobel Prize in physics.

The Union Carbide Corporation has announced the appointment of JAMES F. EVERSOLE as vice president of the Union Carbide Development Company and of FREDERICK H. ROBERTS as vice president, research, of the Bakelite Company. Both companies are divisions of the corporation. Eversole was formerly vice president, research, of Bakelite; Roberts has been director of research for the Bakelite laboratory in Bloomfield, N.J., since 1955.

CHARLES N. MOORE, professor emeritus of mathematics at the University of Cincinnati, is visiting professor of mathematics at Antioch College during the winter and spring quarters.

JEREMY N. MORRIS of London, England, is serving as visiting professor of epidemiology at the Yale University School of Medicine until March. During his stay, he is participating in the teaching of epidemiology and in developing a comprehensive plan of instruction for the coming years. Morris is director of the Social Medicine Research Unit of Great Britain's Medical Research Coun-

cil, where he is responsible for projects dealing with the epidemiology of coronary heart disease and mental disease.

Another appointment at Yale is that of ROBERT H. GREEN as associate professor of preventive medicine. Green was previously a member of the Yale faculty in the department of medicine, 1947–53. His teaching and research will be concerned with influenza, adeno-, and other respiratory viruses.

WENDELL A. LANDMANN, chemist who since 1951 has held research positions with Armour and Company and with Argonne National Laboratory, has joined the staff of the American Meat Institute Foundation at the University of Chicago as chief of the division of analytical and physical chemistry. He assumes responsibilities previously administered by D. M. DOTY, who wishes to devote full time to his post as associate director of research and education for the institute.

The following Sigma Xi national lecturers will speak at a number of colleges and universities during January, February, and March: A. C. REDFIELD, senior oceanographer emeritus at the Woods Hole Oceanographic Institution, Woods Hole, Mass., will discuss "The Proportions of Things in the Sea," and JOHN T. WILSON, professor of geophysics at the University of Toronto, Toronto, Canada, will discuss "Geophysics and Continental Evolution."

WAYNE H. JENS, formerly project engineer for the Nuclear Development Corporation of America, White Plains, N.Y., has been named assistant technical director at Atomic Power Development Associates, Inc., Detroit, Mich., a nonprofit corporation concerned with research and basic design for the Enrico Fermi Atomic Power Plant now under construction near Monroe, Mich.

The following scientists from England are visiting North America:

J. B. ASHLEY, senior registrar in pathology at the David Lewis Northern Hospital, Liverpool, will be at the Armed Forces Institute of Pathology, Washington, for about a year, beginning in mid-February, to study tumors of the testes.

H. G. DAVIES, of the Medical Research Council's Biophysics Research Unit, King's College, London, is at the Rockefeller Institute for Medical research in New York on a year's leave of absence to work with Keith R. Porter.

GLENN E. ULLYOT, an associate director of research at Smith Kline & French Laboratories, received the 1957 American Institute of Chemists' honor scroll award at a dinner meeting on 9 January at the Penn Sherwood Hotel, Philadelphia, Pa. The Pennsylvania Chapter of the institute gives the award annually for outstanding contributions to the profession.

R. A. DAY, JR., professor of chemistry at Emory University, has been named chairman of the department.

OTTO J. RAMLER, head of the department of mathematics at Catholic University of America, and faculty member for 44 years, has retired from academic service. RAYMOND W. MOLLER is serving as acting department head.

ELLIOTT SHAW, formerly with the Rockefeller Institute, has joined the Tulane University Medical School faculty as associate professor of biochemistry.

RAYMOND E. VANDERLINDE, associate professor of biochemistry at the University of Maryland School of Medicine, has been appointed clinical biochemist in charge of the laboratory at Syracuse Memorial Hospital. Vanderlinde will also serve as assistant professor of biochemistry at the State University of New York College of Medicine.

Recent Deaths

CHARLES F. BROOKS, Cambridge, Mass.; 66; professor emeritus of meteorology at Harvard University; director of Harvard's Blue Hill Observatory in Milton, Mass., 1931–57; founded the American Meteorological Society in 1919 and was one of group who established the Mount Washington Observatory in the White Mountains of New Hampshire; 8 Jan.

ALBERT E. CLEGHORN, Scarsdale, N.Y.; 52; chemist and president of the National Aniline Division of the Allied Chemical and Dye Corporation; formerly taught chemistry at Long Island University; 9 Jan.

SERGE GLUHAREFF, Stratford, Conn.; 54; assistant engineering manager in charge of research and development for Sikorsky Aero Engineering Corporation; developer, with Igor Sikorsky, of amphibious planes; 9 Jan.

W. R. GRAHAM, Toronto, Ont., Canada; 82; poultry specialist; professor at Ontario Agricultural College for 41 years; one of the founders of the Poultry Science Association, from which the World Poultry Science Association grew; 8 Jan.

WALLIE A. HURWITZ, Ithaca, N.Y.; 71; mathematician, professor emeritus at Cornell University; editor of several mathematical journals.

FREDERICK C. IRVING, Belleair, Fla.; 74; obstetrician at Harvard Medical School; formerly governor of the American College of Surgeons; 24 Dec.

KENNETH L. MARK, Boston, Mass.; 83; chemist and former director of the School of Science at Simmons College; taught chemistry at Simmons for 40 years before his retirement in 1940; 12 Jan.

VELMA D. MATTHEWS, High Point, N.C.; 53; head of the biology department of Coker College in Hartsville, S.C., since 1935; 7 Jan.

FREDERICK W. MERRIFIELD, Chicago, Ill.; 70; pioneer in facial surgery; professor emeritus of surgery at Northwestern University Dental School and associate professor emeritus at Northwestern's Medical School.

HENRY M. MOSES, Brooklyn, N.Y.; 82; a retired physician who had practiced in Brooklyn for more than 50 years; former chief of staff at Peck Memorial Hospital, chief of medical services at Kings County Hospital; professor emeritus of clinical medicine at Long Island College Hospital; 11 Jan.

MIKHAIL A. PAVLOV, Moscow, U.S.S.R.; 95; member of the Soviet Academy of Sciences; metallurgist who in 1946 received a Stalin Prize for his study of the properties of cast iron; 10 Jan.

LELAND S. RHODES, University Park, Pa.; 68; professor emeritus of civil engineering at Pennsylvania State University; 11 Jan.

EDMUND SCHULMAN, Tucson, Ariz.; 49; tree-ring specialist who found in California a group of bristlecone pine trees more than 4000 years old; dendrochronologist of the University of Arizona Laboratory of Tree Ring Research since 1932; formerly associated with astronomical and meteorological observatories at Harvard University and on the West Coast; 8 Jan.

MARCELLUS H. STOW; Lexington, Va.; head of the department of geology at Washington and Lee University; past president of the Virginia Academy of Science; 27 Nov.

LESTER C. SWICKER, Brookside, N.J.; 61; electrical engineer at Bell Telephone Laboratories in Murray Hill, N.J.; 8 Jan.

WILLIS R. WHITNEY, Schenectady, N.Y.; 89; former director of the General Electric Industrial Laboratory; nonresident professor of chemical research at Massachusetts Institute of Technology; 9 Jan.

JOHN T. WILLIAMSON, Mwadui, Tanganyika; 50; Canadian geologist; owner of largest private gem claim; discoverer of the richest privately owned diamond mine in the world; 7 Jan.

THOMAS L. YORK, Ithaca, N.Y.; 36; associate professor of vegetable crops and plant breeding at Cornell University; 21 Dec.

Reports

Archeological Investigation of Cuicuilco, Valley of Mexico, 1957

Between 28 May and 8 July 1957, a National Geographic Society–University of California expedition conducted explorations in the archeological zone of Cuicuilco, D.F., Mexico. The party included, in addition to us, A. B. Elsasser, René Millon, and R. J. Squier of the University of California and Eduardo Contreras of the Instituto Nacional de Antropología e Historia (*1*). Recently instituted commercial quarrying of the lava flow (pedregal) which overlies the archeological deposits disclosed several earth mounds. These were recognized as of archeological significance by Eric Wolf and Angel Palerm in 1956 (*2*).

By January 1957, the sloping sides of four small earth mounds had been partially exposed by clearing off the superjacent basalt in quarrying operations. In each case the lava flow had not completely covered the top of the mounds, which anciently formed obstructions to the flow. One edge and the center of each mound was available for excavation, and testing of three of the mounds was carried out. Each mound proved to contain a structure, either of clay or earth, with a basalt boulder facing, as well as graves, an abundance of potsherds, and minor artifacts. The mounds thus far located in the quarry area lying on the west side of Insurgentes Boulevard have been grouped by us as a separate subzone of Cuicuilco, and will be referred to as Cuicuilco-B in order to distinguish it from the Cuicuilco Pyramid itself (lying about 0.3 mile to the east) which was the scene of Cummings' investigation.

That Cuicuilco-B is contemporaneous with and associated with the round, terraced, boulder-faced Cuicuilco Pyramid is established beyond question. It thus appears that the pyramid and Cuicuilco-B complex as a unit may represent the beginnings of urbanism, which would be the earliest such development now known for the Central Mexican Highland. The extent of the site complex is clearly greater than now known, and only with additional quarrying can the full extent and arrangement of the various components be determined.

Mound 1 contains a clay platform mound, probably oval in outline, rising 7 meters above the base in a series of narrow curved terraces which are smoothly surfaced. The size of this structure was not determined, but its minimum length is over 100 feet. The history of the structure is complicated since the original low structure which rested on tepetate subsoil was rebuilt three times by adding to its lateral and vertical dimensions. It is believed that this clay platform mound is earlier than the stone-faced structures in mounds 2 and 4 (see below) and that, in all probability, the innermost structure in the Cuicuilco Pyramid may be a clay construction of this sort.

Mound 2 yielded a square platform measuring 48 feet on a side with sloping sides which were faced with basalt cobbles. The hearting of the structure consisted of a fill of midden deposit probably secured in the immediate vicinity. The original platform was enlarged once, and at this time a row of well-dressed rectangular granite blocks was laid down as a decorative feature.

Mound 4 is less completely known since only a single trench was excavated. This excavation disclosed a basalt boulder facing about 3 feet thick covering the outside of the conical earth mound. An inner structure consisting of what seems to be a rectangular pit whose sides are lined with basalt boulders contained a circular clay basin, numerous thin sand and ash layers, much charcoal, and an abundance of sherds. Two burials in this stone-lined pit were associated with large numbers of the distinctive cruciform objects recorded earlier by Kroeber (*3*). These are hand-modeled flat four- or six-pointed objects made of white wood ash.

The clay and stone-faced structures in mounds 1, 2, and 4 were apparently abandoned and suffered erosion of their crowns for some period. Terminal use of the Cuicuilco-B area is marked by occupation debris lying on top of the eroded structures and immediately beneath the pedregal. A similar sequence of events apparently occurred at the pyramid, according to Cummings (*4*). Constructions employing unfired adobe bricks which occur in the pyramid were not noted in mounds 1, 2, and 4.

An abundance of potsherds and a few complete vessels were recovered from the three excavated mounds. Small collections were obtained from the midden sheet lying beneath the lava between the mounds and from the bottom of the 21-foot-deep shaft previously excavated by Cummings near the pyramid. This material has not yet been fully analyzed, but the following tentative observations can be made.

The crown of each mound, which remained uncovered by lava, yielded Aztec sherds mixed with earlier Preclassic refuse. Sherds recovered from the capping deposit between the platform constructions and the lava which covered the mound slopes appear to date from the very end of the Preclassic period and suggest the contemporaneity of the Ticoman III and Teotihuacan I periods. Deeper deposits, especially near the base of the clay platform (mound 1), produced only Ticoman III sherds; it is possible that earlier phases may be revealed when the analysis is completed.

Burnished utility ware, including ollas and several large bowl forms, comprises the great majority of sherds. The color ranges from buff through reddish brown to brownish black, while the rim forms show the complete range found in the Ticoman III period (*5*). Loop handles are common but neck handles are quite rare. A variety of smaller bowl forms with burnished interior and exterior surfaces display a similar color range and an emphasis on composite silhouette shapes.

The predominant decorated ware is Ticoman III red on yellow, but Ticoman incised red on yellow is relatively rare. Dull white ware is common in contrast to a much rarer polished white ware. Polychrome painting is poorly represented. Other Ticoman III decorated wares include red, red on brown, red on white, black on white, white on red, black, several yellow-to-orange wares, and a variety of types which feature incised, cuneiform, fabric-impressed, channeled, or notched-ridge decoration. A wide range of tripod supports were found, including globular (most common), double globular and true mammiform (very rare), globular with cusp, conical, claw, and naturalistic leg forms comparable to those of Ticoman (*6*) and Gualupita (*7*).

The latest sublava deposits yielded a sizable sample of sherds which suggest

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All technical papers and comments on them are published in this section. Manuscripts should be typed double-spaced and be submitted in duplicate. In length, they should be limited to the equivalent of 1200 words; this includes the space occupied by illustrative or tabular material, references and notes, and the author(s)' name(s) and affiliation(s). Illustrative material should be limited to one table or one figure. All explanatory notes, including acknowledgments and authorization for publication, and literature references are to be numbered consecutively, keyed into the text proper, and placed at the end of the article under the heading "References and Notes." For fuller details see "Suggestions to Contributors" in *Science* **125**, 16 (4 Jan. 1957).

either a transition from the ceramic tradition of Tiquisman to that of Teotihuacan or the influence at Cuicuilco of developing Teotihuacan from some other part of the Valley of Mexico. The most distinctive and abundant ware bears negative painting (black on yellow or black and red on yellow) with more complex, less curvilinear designs than are typical of Teotihuacan I negative. One type of vessel support has a Teotihuacan I form (*8*) but the surface lacks the characteristic high polish. Several other wares, including red, red on yellow, white on red, and blackish brown, display decorative designs, forms, or high polish which are related in some manner as yet incompletely understood to standard Teotihuacan I types.

Definite Teotihuacan I sherds are rare and occur in the uppermost levels. These include a scattered assortment of red, negative, polychrome, and fine-line incised types.

A small sample of very thin polished red and polished black sherds from the base of Cummings' shaft near the pyramid and from the deepest levels of mounds 2 and 4 may represent an earlier ceramic period. These are possibly related to El Arbolillo, but no firm conclusion on this is possible until the material has been analyzed further.

A variety of clay figurines support the conclusion on a terminal Preclassic date. Three radiocarbon dates are available for Cuicuilco. De Terra collected a subpedregal carbon sample (No. C-200) from the vicinity of the pyramid which yielded a date of 2422 ± 250 years. In January 1957, two wood charcoal samples (Nos. M-663 and M-664) from below the pedregal were collected from occupation deposits near mound 2 at Cuicuilco-B, and these have been dated by the University of Michigan Laboratory as 2040 ± 200 and 1430 ± 200 years old, respectively. Since samples M-663 and M-664 should be the same age, it seems probable that a laboratory error was made in treating one or both samples. Of the two, the oldest (M-663) is more likely to be closer to the actual age. Piña Chán's date for the termination of the Preclassic (Formative) in the Valley of Mexico is 200 B.C. (*9*). Since the Cuicuilco-B material seems to be primarily Late Preclassic but is associated with ceramics which are related to Teotihuacan I as known from the sites of El Tepelcate (*8*), the inner hearting of the Pyramid of the Sun at Teotihuacan (*10*), and to the newly discovered Teotihuacan I complex at Teotihuacan (*11*), the date of sample M-663 seems to be more nearly correct than that of M-664.

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31 JANUARY 1958

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1. The assistance of Eusebio Davalos, Ignacio Bernal, and Roman Piña Chán of the Instituto and Carmen Leonard of the Centro de Investigaciones Antropologicas de México is gratefully acknowledged.
2. The National Geographic Society provided funds to support the recent investigations. Their recent interest may be considered a continuation of their earlier interest in the site, which dates from 1922–25, when Byron Cummings investigated the Cuicuilco Pyramid under the society's auspices. The University of California, through the Committee on Research and Associates in Tropical Biogeography, provided further assistance.
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30 September 1957

Electrolytically Controlled Device for Dispensing Liquids

Commercially available equipment for dispensing small volumes of liquids continuously for 24 to 72 hours was considered inadequate, or too expensive or cumbersome for certain applications. An instrument was therefore designed to utilize the production of gas by electrolysis of water for dispensing solutions aseptically and at any desired rate, by regulation of the electric current (*1*).

The unit, shown in Fig. 1, has two chambers, a generator (*A*) holding the platinum electrodes and a reservoir (*B*). The two chambers are separated by a rubber balloon (*C*). Gases generated by electrolytic decomposition of water in the generator apply pressure within the balloon which in turn forces the liquid through the delivery tube (*D*). The 9-mm inner tubing (*E*) eliminates the chance of explosion by separating the oxygen and hydrogen generated by electrolysis. Tube *E* also acts as an automatic cut-off switch by interrupting the circuit when sufficient gas accumulates in tube *E* to fill it below the tip of the movable electrode (*F*).

The electrode section (*A*), including tube *E*, is filled with an electrolyte. After chamber *A* is completely filled, suction is applied at *G* to collapse the rubber balloon (*C*), after which the stopcock is closed. The liquid to be dispensed is placed in chamber *B*, and the air is displaced by allowing balloon *C* to expand into the lower chamber. As soon as all of the air is displaced, *A* and *B* are tightly fitted together, the stopcock is closed again, and the delivery tube (*D*) is opened.

The delivery rate was found to be equal to that calculated by using the electrochemical equivalents of hydrogen and oxygen, with appropriate corrections for temperature and pressure of the gas phase. A current of 1 ma produced 0.0104 ml of gas per minute at 760 mm-Hg and 0°C. A small transformer and selenium rectifier with a potentiometer and milliammeter have been used, but the transformer and rectifier can be replaced by a 6-v battery.

This device has been used for delivering liquids for continuous-flow paper electrophoresis, and for compensation in a Tiselius type electrophoresis apparatus. A modified apparatus, in which the generator was connected to a reservoir by Tygon tubing, was used for controlling flow rates in ion-exchange or chromatographic separations. Either device can be used for continuous adjustment of *p*H or for addition of nutrient solutions to bacterial cultures during growth, as in a chemostat.

Electrolytic production of gas from water to dispense liquids has the following advantages. (i) The rate of flow is almost infinitely variable. (ii) The flow rate can be adjusted easily at any time without disturbing the apparatus assembly. (iii) The liquid is dispensed uniformly. (iv) The cost per unit is much less than the cost of equipment in which a syringe is used to perform analogous operations. (v) Controls may be remote from the actual device, and power requirements are minimal. (vi) The appa-

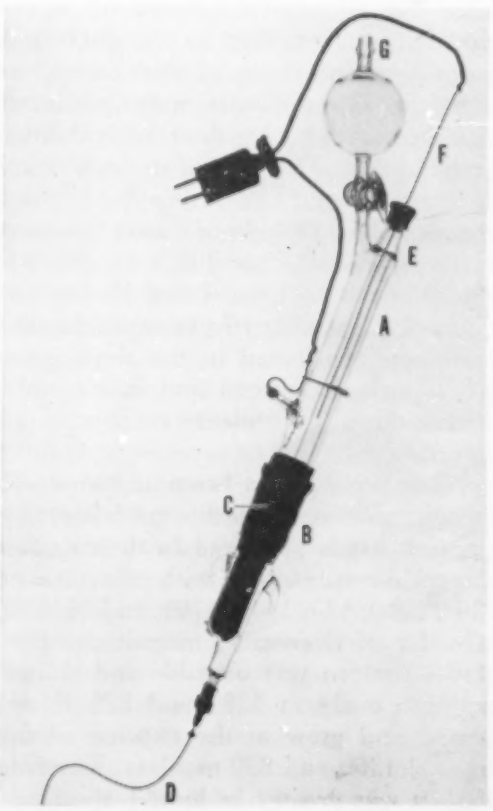

Fig. 1. Electrolytically controlled device for dispensing small volumes of liquid.

ratus can be made small and compact for mounting on individual flasks in an incubator or on a shaker for adding acid, alkali, or other reagents during incubation of bacterial cultures. Only light leads are needed to service the units and, if several units are to be used, as for replicate flasks, addition will be identical in all flasks if the electrodes are wired in series. (vii) There are no moving parts which need lubrication.

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Reference

1. This work was supported by a contract between the University of California and the Office of Naval Research. The opinions contained in this report are not to be construed as reflecting the views of the Navy Department or the Naval Service at large.

23 September 1957

Radiation-Induced Reactions of Potassium Bromide with Air

Pressed discs of potassium bromide (*1*) showed selective absorption in the 4000 to 650-K (*2*) infrared region after irradiation with 1.5-Mev electrons in the presence of air, oxygen, nitrogen, helium, or carbon dioxide. The samples received about 10^{21} ev/g at a dose-rate of about 10^{19} ev/min. In all experiments the potassium bromide "windows" became less transparent as devitrification, with consequent scattering, proceeded. In addition, there was decreased absorbance of the only bands initially present—those centered at 3430 and 1630 K, which were due to adsorbed water or to occluded water retained by the potassium bromide despite careful desiccation, or to both. These results were produced also by heating the discs several hundred degrees. The rate of devitrification decreased as the rate of heating was decreased. The "windows" were restored to the glass-clear condition by repressing. While loss of water and devitrification were the only effects noted for experiments conducted in the three gases last named, in oxygen and in air, radiation-induced chemical reactions occurred.

When a potassium bromide "window" was irradiated in ordinary laboratory air, new bands appeared in the infrared absorption spectrum, with maxima at 1360, 1260, 830, 1440, 1765, and 2340 K, in order of decreasing magnitude. Part of the pattern was unstable and shifted rapidly: peaks at 1385 and 825 K appeared and grew at the expense of the original 1360 and 830 maxima. The rate of shift was greater in humid air. Since the new peaks were characteristic of potassium nitrate dispersed in potassium bromide and in Nujol (*3*), it was interesting to speculate on the precursor. The immediate possibilities were: (i) that scattered "isolated" nitrate ions on the surface of the disc migrated to form potassium nitrate crystals; (ii) that a metastable crystalline phase of potassium nitrate was initially formed on the surface under the influence of the crystalline surface forces of the potassium bromide lattice and subsequently recrystallized. The latter possibility appeared to be the more likely since it was found (*4*) that isotropic, triangular microcrystals of high melting point, which spontaneously changed to the normal anisotropic form of potassium nitrate, were produced on the surface of potassium bromide crystals irradiated in air with polonium alpha rays.

Although nitrogen dioxide alone (the other nitrogen oxides were inert) reacted with potassium bromide in a manner similar to that of irradiated air, the 100-fold greater rate of reaction at room temperature (20-fold greater at 70°C) in the latter case indicated that energy-rich surface dislocations or excited gaseous intermediates were involved in the reaction. At constant dose-rate, it was found that the production of infrared-absorbing species decreased as the contact time of the irradiated air with the salt diminished. Coupled with the fact that discs irradiated in helium at room temperature did not undergo appreciable postirradiation reaction with air, the view that excited gaseous intermediates were involved gained plausibility.

Of the absorption bands listed above, those centered at 1385, 825, and 1765 K could be identified as belonging to potassium nitrate; that centered at 2340 K, which appeared only in windows prepared from chemically pure potassium bromide and not in windows made from Harshaw optical grade potassium bromide, was undoubtedly produced by carbon dioxide arising from the radiolysis of organic impurities; that centered at 1260 K, on the basis of other work (*5*) could be tentatively identified as belonging to potassium nitrite produced by radiolysis of potassium nitrate. Although potassium carbonate has been reported (*3*) to have a very strong absorption band at 1450 K, the 1440 peak here noted did not appear when potassium bromide was irradiated in an atmosphere of carbon dioxide; it did appear when the irradiations were conducted in atmospheres of oxygen or air. Possibly KNO, which has been reported (*6*) to absorb at 1445 K, or KOBr was the absorbing species.

The irradiation of a disc in an atmosphere of dry oxygen produced, in addition to the aforementioned peak at 1440 K, an infrared absorption band with a maximum at 790 K, which was found to be the principal absorption region of potassium bromate when it was dispersed in potassium bromide or Nujol (*3*). This absorption did not appear when the irradiations were conducted in dry or moist air.

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30 September 1957

Mechanism of Immune Hemolysis: Recognition of Two Steps in the Conversion of $EAC'_{1,4,2}$ to E*

In recent publications from this laboratory (*1*) it has been established that the lysis of sheep erythrocytes (E) by Forssman antibody (A) and guinea pig complement (C′) is the result of a series of successive reaction steps, as follows:

$$E + A \longrightarrow EA \quad (1)$$

$$EA + C'_{1,4} \xrightarrow{Ca^{++}} EAC'_{1,4} \quad (2)$$

$$EAC'_{1,4} + C'_2 \xrightarrow{Mg^{++}} EAC'_{1,4,2} \quad (3)$$

$$EAC'_{1,4,2} + C'_3 \longrightarrow E^* \quad (4)$$

$$\text{inactive product} \quad (4a)$$

$$E^* \longrightarrow \text{ghost} + \text{hemoglobin} \quad (5)$$

In this scheme C'_1, C'_2, C'_3, and C'_4 represent the four recognized components of complement (*2*). Ca^{++} and Mg^{++} have been found to function in steps 2 and 3, respectively. E* refers to an activated or damaged cell which eventually hemolyzes without further interaction with complement from the fluid phase. The conversion of $EAC'_{1,4,2}$ to E* by C'_3 has been found to proceed without requirement of a divalent cation such as Ca^{++} or Mg^{++}, and hence can take place in the presence of 0.01*M* ethylenediamine tetraacetate (EDTA). As a source of C'_3, either $C'_{\bar{3}}$ (guinea pig serum lacking C'_1 and C'_4) or whole guinea pig serum in the presence of 0.01*M* EDTA has been used. The identification of C'_3 as the component which interacts with $EAC'_{1,4,2}$ to form E* (*3*) is based on the observation that $EAC'_{1,4,2}$ can be hemolyzed by R_1, R_2, or R_4, but not by R_3 (*4*).

With the aid of a kinetic theory of the mechanism of steps 4 and 4a, it has been shown that both the rate and extent of reaction 4 are dependent on the square of C'_3 concentration (*5*). Since no lag was detected in kinetic analyses of step 4, it was postulated that this process involves a single reaction, that is, a one-hit mechanism. In order to reconcile this with the dependence of rate and extent of reaction on the square of the C'_3 concentration, it was assumed that the process involves two simultaneous hits by C'_3 (*1*) or that the active form of C'_3 is a dimer in equilibrium with an inactive monomer. However, these assumptions have now become unnecessary, for recent experiments have furnished two independent lines of evidence which indicate that the conversion of $EAC'_{1,4,2}$ to E* requires more than one step.

Before this new evidence is presented, it should be pointed out that the observation that $EAC'_{1,4,2}$ can be hemolyzed by R_1, R_2, or R_4, but not by R_3 (*3*), does not necessarily imply that C'_3 is the only component required to transform $EAC'_{1,4,2}$ to E*. The possibility must be considered that the conversion of $EAC'_{1,4,2}$ to E* requires C'_3, as well as another, as yet unrecognized, component of the C′ system. In our earlier work this possibility was dismissed because the process was believed to be a one-hit reaction.

In recent kinetic studies of reactions 4 and 4a, it was discovered that no lag was apparent in the earlier experiments (*1*) because the technique employed to stop the reaction in the samples at the desired times was not adequate. This difficulty was overcome (i) by working in a cold room at about 5°C instead of room temperature, (ii) by diluting the samples 1/11 instead of 1/3 with ice-cold buffer, (iii) by centrifuging immediately in prechilled (5°C) table centrifuges rather than at room temperature, (iv) by pouring off the supernatant fluids immediately after centrifugation, and (v) by resuspending the cells in fresh buffer before further incubation at 37°C, instead of incubating the sedimented cells in the presence of the original supernatant fluid. The use of a 1/11 dilution of the samples was arrived at after several lower dilutions were tested under conditions i, iii, iv, and v, as shown in Fig. 1. This dilution represents the highest dilution feasible under present experimental conditions.

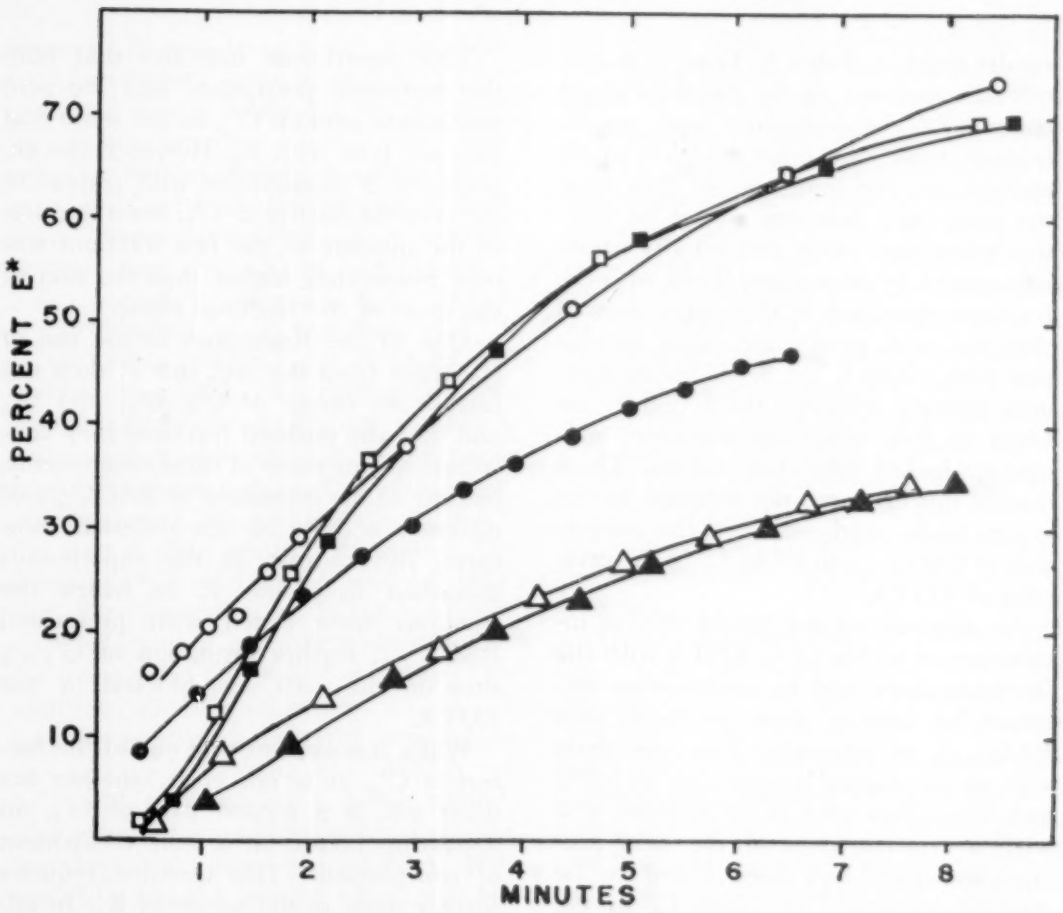

Fig. 1. Kinetics of E* formation from $EAC'_{1,4,2}$. In the descriptions that follow, the term *new sampling method* refers to conditions i, iii, iv, and v described in the text. Open circles: old sampling method, C'_3 1/100 (*10*), experiment No. 082354. Solid circles: old sampling method, C'_3 1/115 (*10*), experiment No. 090154. Open squares: new sampling method, 1.0 ml of sample + 5.0 ml of stopping diluent, C'_3 1/60 (*10*), experiment No. 122156. Solid squares: new sampling method, 1.0 ml of sample + 10.0 ml of stopping diluent, C'_3 1/60 (*10*), experiment No. 122156. Open triangles: new sampling method, 1.5 ml of sample + 3.0 ml of stopping diluent, C'_3 1/90 (*10*), experiment No. 111956. Solid triangles: new sampling method, 1.0 ml of sample + 5.0 ml of stopping diluent, C'_3 1/90 (*10*), experiment No. 111956.

While this new technique may not be perfect, in the sense of effecting complete blockage of further C'_3 action during sampling, it is clear that results obtained in this fashion reflect more closely the actual course of events than do those obtained with the earlier method. With the improved sampling method it was demonstrated that the kinetic curve of E* formation is sigmoidal and not concave to the abscissa as previously claimed (Fig. 1).

This finding indicates that the conversion of $EAC'_{1,4,2}$ to E* involves at least two reaction steps. Hence, an attempt was made to learn, by fractionation of guinea pig serum, whether the components required in these reactions are distinct (*6*). A method was found which led to a separation of two fractions, both of which appear to be necessary for the conversion of $EAC'_{1,4,2}$ to E*. One fraction was obtained by precipitation from whole guinea pig serum on addition of 0.005*M* HCl to *p*H 5.0. After collection by centrifugation, the precipitate was dissolved in 0.04*M* phosphate buffer at a *p*H of 7.1 to a volume equal to the original amount of serum and reprecipitated at *p*H 5.0 with 0.005*M* HCl. The supernatant fluid from the initial precipitation was rendered isotonic and neutral by addition of appropriate amounts of 1.5*M* NaCl and 0.1*M* NaOH. The second fraction was obtained from this solution by addition of methanol to a concentration of 28 percent (by volume). The resulting precipitate was dissolved in a convenient volume (3 to 5 times the original serum volume) of isotonic NaCl and reprecipitated by addition of methanol to 40 percent (by volume). All operations were performed at 0 to 2°C.

Table 1. Reciprocal of the final dilution of reagent required to convert 50 percent of 7.5×10^7 $EAC'_{1,4,2}$ to E* in a reaction volume of 2.5 ml in the presence of 0.01*M* EDTA in 90 minutes at 37°C. In all assays, the cells as well as the C′ fractions were used on the day of preparation.

Expt. No.	*p*H 5.0 ppt.	Methanol ppt.	Mixture	Whole C′
1	< 5	47	260	610
2	36	8	400	720
3	< 5	< 5	260	710
4	95	17	490	720
5	86	18	390	650

The results of five experiments, summarized in Table 1, indicate that the two fractions are far more active in admixture than alone. It appears, therefore, that conversion of $EAC'_{1,4,2}$ to E* requires at least two factors.

However, before this conclusion can be regarded as valid it is necessary to consider the possibility that anticomplementary effects might account for the

results cited in Table 1. Thus, it is conceivable that one of the fractions might contain C'_3 in admixture with an inhibitor, while the other fraction might contain an anti-inhibitor. If this were the case, both fractions would be inactive when used alone, but activity would be restored by admixture. Tests with the fractions described in this paper showed that the acid precipitate, after incubation with whole C′ at 37°C for 30 minutes, strongly inhibited the action of the latter on EA, while the methanol precipitate lacked inhibitory action. These results, however, are not relevant to the system under study—that is, the conversion of $EAC'_{1,4,2}$ to E* by C′ in the presence of EDTA.

An appropriate test would involve incubation of whole C′ in EDTA with the fractions alone and in combination followed by tests of these mixtures with $EAC'_{1,4,2}$ as substrate. This was done with an incubation temperature of 37°C and incubation time of 30 minutes, and with a concentration of the acid precipitate which had been found to be strongly inhibitory to whole C′ in the previous test. No anticomplementary action was observed in the modified test with $EAC'_{1,4,2}$ as substrate, and, indeed, in all cases such treatment enhanced the conversion of $EAC'_{1,4,2}$ to E*.

The results of the fractionation experiments permit two alternative interpretations: (i) Each of the fractions contains a different component of complement; these two components act sequentially to transform $EAC'_{1,4,2}$ to E*. (ii) One of the fractions contains a component of complement (presumably C'_3) which converts $EAC'_{1,4,2}$ to E* by two successive reactions, while the other fraction contains a cofactor or activator for this process.

Further experiments are needed to distinguish between these interpretations. With respect to the first interpretation, since either R_1, R_2, or R_4 is able to convert $EAC'_{1,4,2}$ to E*, it would appear that both of the factors involved in this reaction are distinct from C'_1, C'_2, or C'_4. Furthermore, since R_3 does not convert $EAC'_{1,4,2}$ to E*, at least one of these factors is C'_3. Attempts were made to reconstitute R_3 (at a nonlytic level) by addition of the alcohol and acid precipitable fractions, alone and in combination (in the proportions corresponding to the original guinea pig serum). The three mixtures, as well as whole C′, were assayed for their ability to hemolyze sensitized sheep red cells (EA) in the presence of Ca^{++} and Mg^{++}. The results were expressed as the reciprocal of the final dilution required to yield 50-percent lysis, as judged by visual inspection, and are given as follows: R_3 + methanol precipitate, 120; R_3 + acid precipitate, 350; R_3 + mixture, 750; whole C′, 1500.

This experiment indicates that both the methanol precipitate and the acid precipitate contain C'_3, in the sense that they are lytic with R_3. However, the experiment is inconclusive with respect to the possible duality of C'_3, since the titer of the mixture of the two fractions was only moderately higher than the sum of the titers of the fractions alone.

One of the limitations in the use of R_3 arises from the fact that it does not furnish an excess of C'_1, C'_2, and C'_4 and that the purified fractions may contribute one or more of these components, leading to the formation of $EAC'_{1,4,2}$ of different activity in the different mixtures. By contrast, in the experiments described in Table 1, in which the fractions were tested with preformed $EAC'_{1,4,2}$, further formation of $C'_{1,4,2}$ sites on the cells was blocked by the EDTA.

While it is evident that one of the factors is C'_3, it is not clear whether the other one is a second part of C'_3, an activating factor, or a new component of complement. This question requires further study of the nature of R_3. In addition, it is not known whether the two factors act on $EAC'_{1,4,2}$ in a definite sequence. Finally, it will be necessary to reexamine the properties of $EAC'_{1,4,2}$ with the aim of determining whether a population of cells "in the state $EAC'_{1,4,2}$," when prepared as described by Levine, Mayer, and Rapp (*3*), has progressed, at least in part, beyond this stage by interaction with one of the factors. This possibility must be considered since in the preparation of $EAC'_{1,4,2}$ a small proportion of cells is lysed.

In regard to the nature of R_3, it is pertinent that Da Costa Cruz and De Azevedo Penna (*7*), employing conventional C′ reagents, concluded that C'_3 consists of at least two different substances, on the basis of the differential destruction of C'_3 by formaldehyde on the one hand and by sodium hydrosulfite on the other.

There have been quite a few reports presenting evidence of the existence of complement components other than C'_1, C'_2, C'_3, and C'_4 (*8*). Some workers in the field, including the members of this laboratory, have been reluctant to accept the existence of more than four components because of the limitations inherent in the use of serum fractions which are subjected to destructive treatments and which are recombined in order to reconstitute hemolytic activity. The present evidence on a new component or factor of the complement system is not based on the use of reagents prepared by destructive treatment (*9*).

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9. This work was supported by grants from the National Science Foundation and by contract Nonr 248(17) with the Office of Naval Research.
10. It should be noted that C'_3 concentrations are comparable only within a given experiment, since the reactivity of $EAC'_{1,4,2}$, which varies from experiment to experiment, affects the extent of reaction. The reaction mixtures contained 3×10^7 erythrocytes per milliliter and 5.0 ml of the C'_3 dilutions indicated for each experiment in a total volume of 25.0 ml.

24 September 1957

Banana Feeding and Urinary Excretion of 5-Hydroxyindoleacetic Acid

The diagnosis of malignant carcinoid in man can be made by the presence of markedly increased excretion of 5-hydroxyindoleacetic acid (5-HIAA) in the urine. The increased excretion of this acid in the urine of patients with carcinoid tumors is derived from 5-hydroxytryptamine, which is present in very large concentration in the carcinoid tumors (*1*). 5-Hydroxytryptamine is converted to 5-HIAA by the action of aminooxidases (*2*). The range of excretion values for 5-HIAA obtained from carcinoid patients is 21 to 680 mg/day, as compared with 2 to 9 mg/day for adult normal subjects (*3*).

The 5-hydroxyindoles found in the urine of carcinoid patients and of normal man are derived primarily from the metabolism of tryptophan. The excretion in normal man is relatively constant over wide ranges of tryptophan intake. However, addition of very large amounts of tryptophan to the diet of normal man results in increased excretion of 5-HIAA in the urine. A twofold increase in excretion of this acid has been demonstrated following loading with 3.5 g of tryptophan.

To date, the elevated values of

5-HIAA found in the urine of patients with carcinoid tumors have not been observed in other clinical conditions in man. No reports have been found on the influence of dietary constituents other than tryptophan in producing an increase in excretion of 5-HIAA of such a striking nature.

The effect of banana on the excretion of 5-HIAA was accidentally observed. At the conclusion of a study on the excretion of this acid in monkeys maintained on a monkey chow diet, a banana was given on the final day as a reward for satisfactory performance. Surprisingly, a 24-fold increase in the 24-hour excretion of 5-HIAA was found in this final urine sample. This observation led to the studies described in this report.

Twenty-four-hour urine specimens were collected from four rhesus monkeys. The excretion of 5-HIAA was measured by means of the method of Udenfriend, Titus, and Weissbach, which is presumably highly specific for this acid (4). The 5-HIAA excreted during control periods has been compared with that observed following the feeding of banana. Iproniazid (1-isonicotinyl-2-isopropylhydrazide) is capable of blocking the action of monoaminooxidases, both in vivo and in vitro (5). The effect of the administration of iproniazid on the excretion of 5-HIAA was observed in the monkeys during the feeding of a normal monkey chow diet and during the period of addition of banana to the diet. The results are presented in Table 1.

The excretion of the acid during control periods was relatively constant. Feeding of banana produced a prompt rise in the amount of acid excreted. Addition of 50 to 150 grams of banana to the diet resulted in acid excretion of from 5 to 30 times the values obtained for control periods.

The administration of iproniazid (50 mg/kg intraperitoneally twice daily, at 8 A.M. and at 4 P.M.) resulted in a marked reduction in the excretion of the acid. Decreases to 0.1 that observed for the control period occurred by the second day of iproniazid administration. The acid excretion returned to normal values within 48 hours after discontinuation of the iproniazid administration.

Iproniazid was administered to the monkeys following 4 days of banana feeding (150 g of whole banana per day). A prompt decrease in excretion of the acid occurred. This was progressive throughout the 3 days of iproniazid administration. In spite of banana feeding, iproniazid appeared to return the excretion value to control, or low control, values. Three days after discontinuation of both banana and iproniazid, the excretion values had returned to the average for control periods.

A similar effect of banana feeding was observed in one 10-year-old male child with recurrent thrombocytopenic purpura and in one 9-year-old female child with phenylpyruvic oligophrenia. The range of 24-hour urinary excretion values in a child with thrombocytopenic purpura, when maintained on a normal hospital diet, was 1.57 to 2.04 mg for a 3-day period. Feeding 300 g of banana a day resulted in an excretion of 13.3 to 18.0 mg of 5-HIAA per 24 hours.

The child with phenylpyruvic oligophrenia excreted an average of 0.66 ± 0.81 mg/day while she was on a general hospital diet for 6 days. The addition of approximately 300 g of banana daily for the next 3 days resulted in urinary excretion values of 7.2, 5.7, and 4.0 mg/day. The excretion of 5-HIAA in this child when on a low phenylalanine diet for 8 days was 0.93 ± 0.38 mg/day. The addition of approximately 200 g of banana per day to this diet resulted in an average excretion of 5-HIAA of 5.77 ± 2.9 mg/day for a 5-day period. The effect of iproniazid in blocking the increased excretion of 5-HIAA produced by banana feeding which was observed in monkeys was also observed in this child. Large oral doses of iproniazid were required; 5 mg/kg per day for 6 days produced no reduction in the excretion values. However, doses of 25 mg/kg for 2 days reduced the 24-hour excretion value to 0.80 mg/day.

Extraction of fresh banana skin, fresh banana pulp, or whole banana baked at 100°C for 2 hours failed to reveal evidence of nitrosonaphthol reacting materials. However, banana pulp that was autoclaved at pressure of 15 lb/in.^{2} and at 250°F, when fed to two monkeys, produced a striking rise in the amount of 5-HIAA in the urine. The administration of large doses of ascorbic acid, or of neomycin sufficient to produce a relatively sterile intestinal tract, did not influence the excretion of the acid in monkeys on a control monkey chow diet or in monkeys on a diet in which banana was fed.

Urine, obtained from a monkey that had been fed banana, and containing approximately 10 µg of 5-HIAA per milliliter, was extracted by the method of Udenfriend into ether. Volumes containing approximately 12 µg of the acid were placed on No. 1 Whatman paper for descending chromatographic analysis, with 5-HIAA as the reference standard. The solvent consisted of isopropanol, water, and ammonia (200:20:10). Identical spots at the same R_f as the standard 5-HIAA were obtained follow-

Table 1. Effect of banana feeding and administration of 1-isonicotinyl-2-isopropyl hydrazide (IIH) on urinary excretion of 5-hydroxyindoleacetic acid (5-HIAA) in monkeys.

Item	Monkey 510		Monkey 513		Monkey 514		Monkey 405	
	Days	5-HIAA (µg/hr day)	Days	5-HIAA (µg/hr day)	Days	5-HIAA (µg/hr day)	Days	5-HIAA (µg/hr day)
Control	5	1.6 ± 1.0	6	10.4 ± 5.9	6	17.5 ± 2.9	6	10.8 ± 4.7
Banana (50 to 150 g/day)					1	81.8	1	138.9
Banana (50 to 150 g/day)	1	19.0	1	31.8	1	32.3	1	32.0
Banana (50 to 150 g/day)	1	17.1	1	52.4	1	78.3	1	97.5
Banana (50 to 150 g/day)	1	24.1	1	90.7	1	79.8	1	52.4
Banana (50 to 150 g/day)	1	43.2	1	77.6	1	87.1	1	105.8
Banana (50 to 150 g/day)					1	76.9	1	72.5
Banana (50 to 150 g/day)					1	33.1	1	35.6
Control	3	8.1 ± 1.4	3	19.0 ± 11.3	3	19.4 ± 5.1	3	16.9 ± 5.1
IIH	1	7.6	1	5.8	1	10.0		
IIH	1	1.0	1	1.0	1	3.7		
IIH	1	1.2	1	1.9	1	2.1		
IIH					1	4.0		
Control	1	4.0	1	3.3	1	10.9		
Control	1	3.1	1	17.3	1	17.0		
Banana (150 g/day)	4	25.8 ± 11.8	4	63.1 ± 26.2	7	67.1 ± 23.8	7	76.4 ± 39.6
Banana + IIH	1	14.3	1	28.5	1	32.2	1	7.7
Banana + IIH	1	14.1	1	22.1	1	7.2	1	1.0
Banana + IIH	1	3.2	1	4.3	1	4.9	1	1.1
Control	1	3.8	1	8.8	1	1.4	1	7.2
Control	1	4.7	1	3.1	1	45.2	1	21.7
Control	1	11.3	1	13.4	1	14.8	1	12.0
Control					1	9.3		

ing color development with *p*-dimethylaminobenzaldehyde in HCl · acetone as well as with nitrosonaphthol in nitrous acid.

The ability of iproniazid to block the increased excretion of 5-hydroxyindoleacetic acid induced by banana suggests that oxidative deamination of this precursor of the acid occurs. These increases in excretion of 5-hydroxyindoleacetic acid in monkeys and in the two children, induced by banana feeding, are of the order observed for certain adult patients with carcinoid tumors and could lead to erroneous diagnosis.

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28 October 1957

Response of Single Cells in Monkey Lateral Geniculate Nucleus to Monochromatic Light

The lateral geniculate nucleus of the rhesus monkey (and of man) consists of six layers of cells separated by fiber layers. Three of these layers receive impulses from one eye, three from the other eye. Thus the visual fibers from each eye split three ways in the thalamus.

We have been investigating the functional significance of the lamination of the lateral geniculate nucleus and, in addition, the nature of the responses of color-selective cells at the thalamic level. The problems of human color vision—for example, the number of color systems and their spectral sensitivities—have been widely debated. The question of whether the systems operate independently, as Helmholtz maintained, or in opposing, complementary pairs, as suggested first by Hering, has never been satisfactorily decided. By tapping in on the visual messages as they are transmitted to the cortex, it should be possible to answer some of these questions.

Granit and his coworkers (*1*) have recorded from single ganglion cells in the retinae of numerous subprimate vertebrates. While the results of these experiments are very interesting and important, the applicability of the results to problems of human vision is limited by the fact that the primate visual system differs in many respects from that of other vertebrates: the most commonly studied animal, the cat, is, for instance, nocturnal and color-blind. It would seem more appropriate to study the mechanisms of human vision on an animal, such as the rhesus monkey, whose visual system (including color vision) closely approximates that of man.

Five monkeys have been used in this experiment (*2*). The animal, under barbiturate anesthesia, is held in a stereotaxic instrument. A tungsten microelectrode (*3*) with a tip diameter estimated to be from 1 to 3 μ is lowered by a micrometer drive until a single cell of the lateral geniculate nucleus is isolated. The output of the microelectrode, with reference to an indifferent point on the skull, is fed by way of a cathode follower to a conventional amplifying, recording, and monitoring system.

Each of the monkey's eyes is stimulated by one beam of a dual-beam optical system; a beam of light from each side of a ribbon-filament lamp is passed through a shutter and collimated before it is passed through monochromatic interference filters and neutral-density filters. The beams are then focussed on the eyes. This makes it possible to stimulate either eye with any of a number of different wavelengths of variable intensity and duration. Customarily, we adjust the intensity of the light passed by each monochromatic filter so that equal amounts of physical energy are transmitted by each filter. The number of spikes elicited by each monochromatic light stimulus gives a direct indication of the spectral sensitivity of the element under study. The locations of the cells recorded from are estimated from histological analyses of electrode tracks and of coagulation marks made at the end of each experiment.

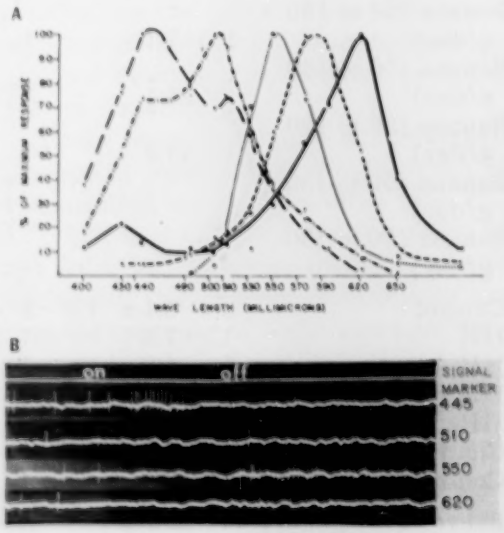

Fig. 1. Responses of single units in the lateral geniculate nucleus. (Top) Response curves for five different types of cells in the dorsal layers. (Bottom) Response of an intermediate-layer cell to four different wavelengths of monochromatic light.

In an earlier experiment (*4*) in which larger electrodes were used, we found that the patterns of responses from the laminae of the lateral geniculate nucleus differed from one another. On-responses were found in the dorsal layers; in the most ventral pair we observed a striking inhibition of spontaneous activity followed by an off-response when the light was turned off. The responses obtained from the two intermediate layers, although more difficult to interpret, appeared to be a combination of the dorsal and ventral types, with on- and off-bursts. Our current single-cell recordings support these earlier findings on different types of responses in the various layers.

Among the cells in the dorsal pair of laminae, we have found some that respond to various narrow ranges of wavelengths in different parts of the spectrum. In our work to date we have found cells with peaks at five different points in the spectrum. In Fig. 1*A* are shown curves of the spectral sensitivity of the different types of elements we have found. These results should be considered preliminary since we have recorded so far from only 66 of the thousands of geniculate cells. The peak at 510 mμ corresponds to the sensitivity of the scotopic system, and presumably it represents mainly a rod connection. The other four presumably correspond to the various color-vision elements. It should be noted that the "blue" cell has a secondary peak at 510 mμ; this is true of all the "blue" cells we have isolated so far and, together with the secondary peak in the blue of the 510 mμ cell, may indicate that "blue" receptors and rods feed into the same neural pathways. In the case of cells with other sensitivities, we have also often found ones with multiple peaks, red and green being a particularly common combination.

Thus there seems to be a complete color-vision system represented in the two dorsal layers of the lateral geniculate nucleus. This is in contradiction to Le Gros Clark's hypothesis (*5*) that each pair of laminae receives impulses from only one of the three classical color receptors, the top layers, for example, containing only "red" cells, the middle "green," and the bottom "blue."

In some ways, the responses recorded from certain cells in the two middle laminae of the lateral geniculate nucleus are even more interesting. Here we have located cells which fire either on- or off-responses, depending on the wavelength of the light. In Fig. 1*B* is a record from one of these cells. It can be seen that the cell gives a large on-response to blue light, little response of any sort to green light, but gives a substantial off-response to greenish-yellow light. We have similarly found "red-on,

green-off" cells. This raises the intriguing possibility that there may well be a second type of color-vision system represented in these layers, one perhaps having to do with such phenomena as afterimages and contrast.

The majority of cells recorded from in this intermediate pair of layers, however, are pure off-cells. We have not had the opportunity to study these layers or the inhibitory ventral layers to the same extent as we have the dorsal layers, but work on them is continuing.

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14 November 1957

Complex Nature of the Step in Immune Hemolysis Involving Third Component of Complement

The immune hemolytic reaction is complex because complement (C′) consists of four recognized components (C'_1, C'_2, C'_3, and C'_4) (*1*). As a result of the elegant studies of Mayer and his coworkers (*2*), the mechanism of immune hemolysis involving guinea pig C′ and sensitized sheep erythrocytes is considered to comprise the following sequence of steps:

$$E + A \rightarrow EA \quad (1)$$

$$EA + C'_1 + C'_4 \xrightarrow{Ca^{++}} EAC'_{1,4} \quad (2)$$

$$EAC'_{1,4} + C'_2 \xrightarrow{Mg^{++}} EAC'_{1,4,2} \quad (3)$$

$$EAC'_{1,4,2} + C'_3 \rightarrow E^* \quad (4)$$

$$E^* \downarrow \text{inactive product} \quad (4a)$$

$$E^* \rightarrow \text{ghost} + \text{hemoglobin} \quad (5)$$

where EA represents a sensitized cell, $EAC'_{1,4}$ and $EAC'_{1,4,2}$ represent cells in a state resulting from interaction with C'_1 and C'_4, and C'_1, C'_2, and C'_4, respectively, and E* represents an activated cell which lyses in the absence of C′.

In a comparative study of inhibitors in several sera and of the effect of these inhibitors in the step involving C'_3 (reaction 4), it was found that the titration curve for C'_3 depended on the source of C'_3. This titration was carried out by the addition of different volumes of a given serum to a fixed concentration of $EAC'_{1,4,2}$ in the presence of 0.017*M* disodium ethylenediaminetetraacetate (EDTA). Disodium ethylenediaminetetraacetate was added to prevent further reaction of C'_1, C'_2, and C'_4 with the cells (reactions 2 and 3). Typical titrations for C'_3 of human, pig, and guinea pig sera are given in Fig. 1, which shows that pig serum gives the greatest limiting extent of hemolysis, although at low concentrations it is not as effective as guinea pig serum. Human serum shows only a trace of activity in this system. One would expect, irrespective of the concentration of C'_3, that the final extent of hemolysis would depend only on the fraction of cells in the state $EAC'_{1,4,2}$ which require presumably only C'_3 for lysis. Therefore, the titration curves for all sera would be expected to have a common limiting end point.

In an attempt to account for these differences, the role of inhibitors in this step was investigated (*3*). The addition of sheep serum to guinea pig serum produces inhibition at this step, resulting in a decrease both in the initial slope and in the limiting value of the curve. The differences observed at low concentrations in the curves for pig and guinea pig sera (Fig. 1) might therefore be explained by the presence of inhibitors in pig serum (*4, 5*). However, these same inhibitors cannot be invoked to explain the intersection of these curves and the greater extent of hemolysis produced by high concentrations of pig serum.

Pig serum was heated at 56°C for 15 minutes to destroy C'_1 and C'_2 activity and titrated together with normal pig and guinea pig sera. Heating the pig serum had only a slight effect on its reactivity with $EAC'_{1,4,2}$, and the limiting extent of hemolysis obtained remained greater than that obtained with normal guinea pig serum. Evidently C'_1 and C'_2 are not responsible for the increased reactivity of pig serum.

Classical reagents for the titration of the components of C′, namely R_1, R_2, and R_4, which are deficient in C'_1, C'_2, and C'_4, respectively, were prepared from pig serum (*6*) and titrated. The results are shown in Fig. 2. These reagents, which are nonhemolytic when added to equivalent concentrations of sensitized cells, gave final extents of hemolysis greater than that of normal guinea pig serum. This confirms the observation that C'_1 and C'_2 are not involved and indicates that C'_4 is probably not responsible either.

Pig serum was fractionated by column electrophoresis on powdered cellulose. One fraction, which was found among the β-globulins, did not lyse $EAC'_{1,4,2}$ in the presence of EDTA, but it enhanced the activity of guinea pig serum in this system. Pig serum therefore contains a factor which reacts in the presence of EDTA and is responsible for the increased activity of pig C′.

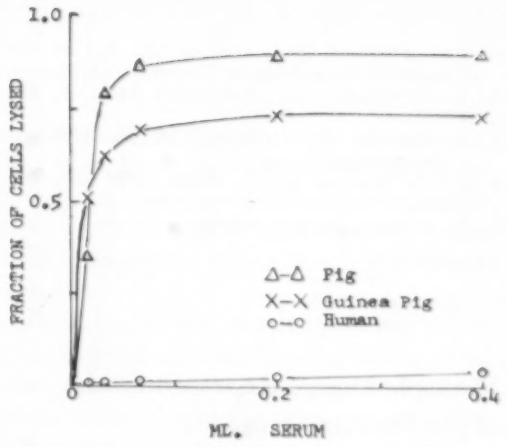

Fig. 1. Lysis of $EAC'_{1,4,2}$ with different sources of C'_3.

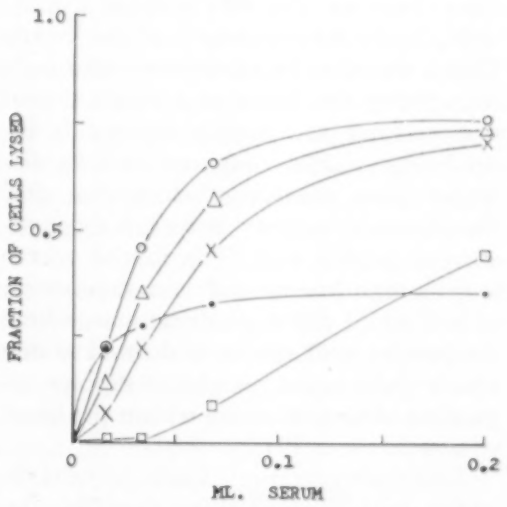

Fig. 2. Lysis of $EAC'_{1,4,2}$ with classical reagents derived from pig serum compared with lysis with guinea pig and pig sera. Open circles, pig serum; triangles, R_4 reagent; crosses, R_1 reagent; squares, R_2 reagent; solid circles, guinea pig serum.

The lysis of $EAC'_{1,4,2}$ appears, therefore, to involve a component, other than C'_3, whose properties do not coincide with those of C'_1, C'_2, or C'_4. This component, necessarily present in guinea pig serum, is not reactive in the presence of 0.017*M* EDTA, while its counterpart in pig serum is active. In this respect it differs from the dual C'_3 factors that Rapp (*7*) found in guinea pig serum, which, when mixed, are active in the presence of EDTA.

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tion presented by one of us (K. A.) to the Faculty of Pure Science, Columbia University.
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5 August 1957

Multiple Dipole Representation of the Human Heart for Vectorcardiography

Vectorcardiography has progressed to the point where designers of lead systems claim to take into account a multiple dipole representation of the heart. This is stated to be an improvement over considering the heart as a single dipole source, since the heart's volume is indeed appreciable compared with its distances from measuring electrodes, and the electrical activity is spread throughout the heart's wall. The spatial vector loop is then interpreted as a summation of individual dipole contributions, where the perfect lead system is defined as one which gives equal weight to dipoles regardless of their location within the heart volume.

This interpretation leads to pitfalls which bear investigation. Actually, the resulting loop does not contain all the available information concerning a complex heart generator but, indeed, it responds to only the dipole component of such a generator. Only if the heart can be accurately represented by a single dipole of fixed location can a vector loop by itself completely describe its electrical behavior. It is a common misconception among vectorcardiographers that separately located dipole sources can accurately be accounted for by the locus of a single vector loop; for if this were true the next logical (and legitimate) step would be to attribute the loop to a single equivalent dipole.

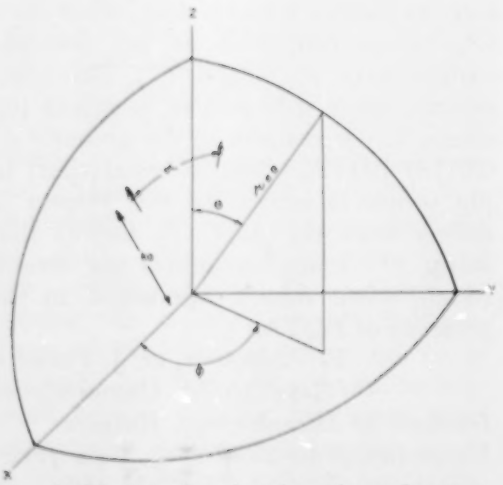

Fig. 1. Sketch showing location of a two-dipole source in a sphere of radius a. The dipoles are located and oriented in the x-z plane. The eccentricity is given by k, which is the percentage of the radius a, and the angular separation is given by α. The positive sense of the dipoles is given by the direction of the arrows, which in this sketch represent radially oriented dipoles; θ is measured from the z axis, and ϕ is measured from the x axis in the xy plane.

The purpose of this study is to show that separately located dipole sources in volume conductors can produce markedly different boundary potentials compared with those produced by a single equivalent dipole source. This single equivalent dipole is assumed to be the dipole component of the complex generator; the difference in boundary potentials represents available information to which the previously defined perfect lead system fails to respond.

Accordingly, boundary potentials produced by two dipole sources in a conducting sphere were calculated and compared with potentials produced by a single equivalent dipole. The equivalence was determined after the Gabor and Nelson (*1*) formulation of equal surface integrals of potential had been applied to a two dimensional disk conductor. The published formulas for two dimensions were found to be in error concerning signs; they should read (*2*):

$$XM_\gamma + YM_x = \gamma \oint V(y\mathrm{d}y - x\mathrm{d}x)$$

$$M_x = \gamma \oint V\mathrm{d}y\,;\; M_y = -\gamma \oint V\mathrm{d}x$$

$$XMy + YM_x = \gamma \oint V(y\mathrm{d}y - x\mathrm{d}x)$$

where X and Y are coordinates of equivalent dipole location; M_x and M_y are the component strength of the equivalent dipole; V is boundary potential; and γ is the conductivity.

When these corrected formulas were applied to two dipoles in a circular disk, the equivalent dipole had a strength equal to the vector sum (taken at the same origin) of the individual dipoles and a location based on a "center of gravity" consideration. When these results were extended to the sphere, the strength of the equivalent dipole was still the vector sum of the two dipole sources, and its location was taken as the "center of gravity" of the two sources (Fig. 1). There is, of course, no assurance that this equivalent dipole or one found by actually performing the indicated integrations for location gives the best match as far as actual surface potentials over the entire sphere are concerned. However, the results show that no single dipole can accurately match the two dipole potentials.

The results are shown in Fig. 2 for radial components and in Fig. 3 for tangential components. Two equal strength dipoles located at 40 percent of the sphere's radius and separated by 60 degrees were used since this represents extreme conditions. It is obvious that large errors are inherent in recording only the single dipole component of a two dipole generator. The errors are larger for radially oriented dipoles than for tangentially oriented ones. The comparisons are, of course, worse for increasing eccentricity and angular separation and are perfect for either zero eccentricity or zero angular separation. It should be noted that, if four radial dipoles are symmetrically placed on a cone of revolution, the comparison is vastly improved. Four dipoles, located and oriented thus, simulate a uniform double-layer source, which Frank (*3*) has shown to be very similar to a single dipole.

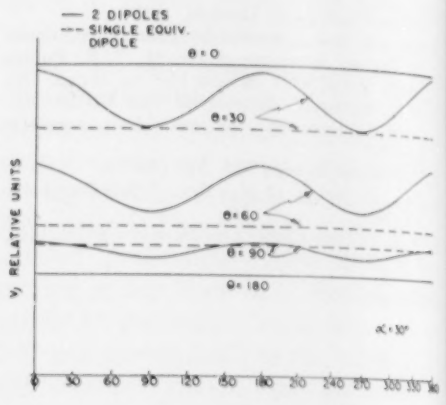

Fig. 2. Potentials over a hemisphere due to two radially oriented dipoles compared with a single equivalent dipole; ϕ and θ are spherical coordinates illustrated in Fig. 1. The dipoles are located and oriented in the planes of $\phi = 0$ degrees and $\phi = 180$ degrees, with an eccentricity of 40 percent of the radius and an angular separation of 60 degrees. The positive sense is away from the origin for both dipoles. Note that $\theta = 0$ and 180 degrees are single points on the sphere surface.

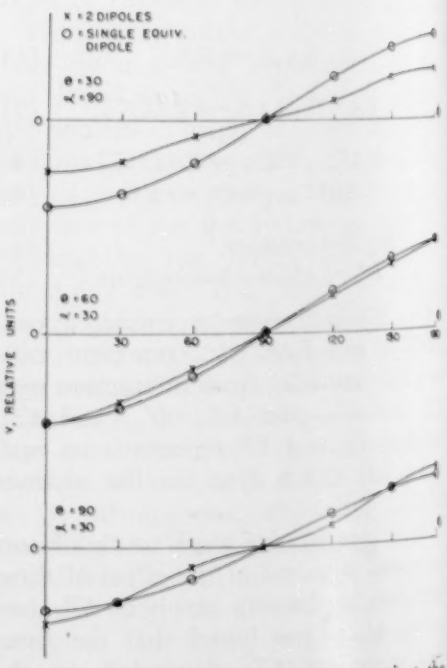

Fig. 3. Same as Fig. 2, except that the dipoles are tangentially oriented with an additive sense.

This study has shown that, *if* the electrical activity of the human heart *cannot* be represented by the action of a single equivalent dipole, a single spatial vector loop by itself cannot possibly contain all the available information. Indeed, if the evidence that diseased hearts are nondipolar is verified, there would be a strong argument for the necessity of some type of precordial scalar leads.

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4. This study was supported in part by research grant H-339-C from the U.S. Public Health Service.

9 April 1957

Equipotentiality Versus Cortical Localization

In an otherwise excellent paper, Weinstein and Teuber recently presented (*1*), without taking specific notice of it, clear-cut evidence that the crux of a possible scientific *synthesis* of the opposite sides of the "equipotentiality-versus-cortical-localization" controversy resides in the different kinds of intelligence for which one tests.

These authors correctly infer that Lashley's (*2*) position tends to be substantiated by their findings that "injury to any lobe of the brain, in either hemisphere, can interfere with performance on certain nonlanguage tasks." Furthermore, they state that Lashley's view of equipotentiality is opposed, as is Rylander's [that is impairment is maximal following injury to the frontal regions (*3*)], by their findings that "performance on a standardized test of 'general intelligence,' such as the AGCT [Army General Classification Test], . . . shows little or no change 10 years after penetrating brain wounds unless the entrance wound included the left parietotemporal region."

They fail, however, to note that this latter statement strongly supports Nielsen's (*4*) views about the validity of the cortical localization concept—that is, that the cortical areas on the *major* side of the brain may be differentiated in terms of their language functions. Moreover, their analysis, as shown in Fig. 1, tends to confound the issue by failing to make specific comparison of the aphasics with the nonaphasics in their experimental sample. Had this been done, the picture of what happens when the left parietal lobe is alone injured would have stood out more clearly.

It appears to me that the results obtained by Weinstein and Teuber could have been predicted from Nielsen's position (*4, 5*), yet no reference is made to him in their article. This is an oversight, because the AGCT seems to be for the most part a test of verbal intelligence (*6*) and, therefore, well suited to testing hypotheses in this area. Their results, which I believe are a solid contribution to the field, happily seem to square nicely with my recent statement (*7*) "that, while there are exceptions on both sides, *animal* experimentation continues to support Lashley's theory of mass action and equipotentiality, but the literature dealing with aphasia in *humans* tends more and more to substantiate Nielsen's confirmation of the classic teaching of cerebral localization. The crux of the disagreement, which by the way is so often overlooked by critics of cerebral localization, is just this: cerebral localization in aphasia deals with language, and language is the most important difference between animals and man"

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4 October 1957

In his comment on our paper (*1*), Holmes emphasizes that our results support a fairly definite localization of language skills in the left hemisphere of the brain. His interpretation is based on a point that we have stressed ourselves, namely that the Army General Classification Test is a verbal instrument. Conceivably even slight traces of aphasia, undetected by other means, might be revealed by inferior performance on the test. We fully agree with Holmes' comment with regard to this possible interpretation.

Holmes further regrets that we fail to compare aphasics with nonaphasics. This comparison was deliberately omitted because of the obvious nature of the results: aphasia is an impairment of language, and the AGCT is a verbal test. However, the comparisons desired by Holmes can be reconstructed from the data contained in our Fig. 1 (*1*). The mean and N of each group are given before and after elimination of aphasics. Thus, the mean drop in score of the group of 10 men (including aphasics) with a left parietotemporal lesion was 18.70. The mean drop in score of the same group after elimination of the four aphasics was 11.17. Arithmetic computation reveals the mean loss of these four aphasics to be 25.01. Incidentally, our Fig. 1 was set up specifically to show "what happens when the left parietal (and other) lobes are alone injured"; what happened was a significant drop in AGCT score after left parietotemporal lesions, and the absence of such a drop after lesions in other parts of the brain.

We find it difficult to follow Holmes when he says that our findings confirm Nielsen's views on localization of function in man. In our brief article we could not enter into the complex history of this field, but it seems clear that a preponderant role of the left hemisphere in man (particularly the left parietotemporal region) for language skills has been observed for nearly a century. In this respect, our findings seem to need no emphasis, since they merely reconfirm what is well known; but just for this reason we cannot see how that laterality difference could specifically support Nielsen's views.

Holmes apparently sees the issues of localization in terms of the classical dichotomy of specific and general effects. He considers Lashley's findings in the rat as an instance of general (nonlocalized) change after cortical removal and invokes Nielsen as an exponent of specificity for man—that is, that every lesion which produces any symptoms produces symptoms of a different kind, depending on its location.

The findings from our laboratory have induced us for some time to reject this dichotomy. Our work has shown rather consistently that brain injuries in man tend to produce twofold effects, "specific" (localizable) and "general" (nonfocal) alterations (*2*). Thus, all subgroups of the population we have studied have shown deficits on certain perceptual

tasks (*3*), regardless of whether the injury was in the right or left hemisphere, or in the frontal, parietal, temporal, or occipital lobes. The deficit on the Army General Classification Test turned out to be comparatively focal (*1*), and so were a number of other changes in performance, such as difficulty with route finding (*4*), which was limited to the group with parietal penetration.

The work of Lashley (*5*) and others on subhuman mammals can be similarly interpreted. For certain complex tasks, such as the maze, Lashley found general (nonlocalized) effects of cortical removals in rats. With other tests, in the same animals, he found focal changes such as alterations in brightness habit after occipital removals, and difficulties on a "double platform box" after anterior removals. Thus, specific and general effects coexist after cerebral lesions in man, as well as in subhuman forms; which of these effects appears to predominate depends on the nature of the tests employed. If the range of the tasks is sufficiently extended, one finds specific and general effects in obligatory association.

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1 November 1957

Thermal Decomposition of 8-Quinolinol Chelates of Silver (I)

The reaction of 8-quinolinol (oxine) with silver (I) has been the subject of a number of investigations. Vis (*1*) found that a green crystalline mass corresponding to the formula, $AgC_9H_6NO \cdot C_9H_6NOH$, was obtained from concentrated solutions of the reactants. Fox (*2*), however, obtained a green precipitate which corresponded to the 1:1 chelate, AgC_9H_6NO. From ionic charge considerations, one would expect the 1:1 chelate to be formed since the 8-quinolinol ion forms a five-membered ring containing one ionic and one covalent point of attachment to the metal ion.

The work of Tzinberg (*3*), which was confirmed by Hein and Regler (*4*), revealed that the formula advocated by

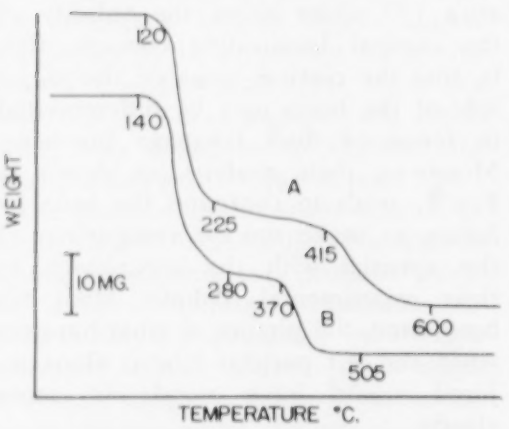

Fig. 1. Thermal decomposition curves of the 8-quinolinol chelates of silver (I). *A*, Green form; *B*, yellow form. Heating rate, 5.4°C per minute.

Vis was correct. Further confirmation came from Block, Bailar, and Pearce (*5*), who were able to prepare two modifications of the chelate, a yellow form and a green one.

The nature of the bonding in the metal chelates is still open to question. It was first thought that silver (I) was oxidized to silver (II) and thus would have the normal bonding found in most of the metal 8-quinolinol chelates. If this were the case, the metal chelates would be paramagnetic; however, it was found that they were diamagnetic and hence, that they were silver (I) chelates (*5*). In view of these findings, it was suggested that the silver chelates were addition compounds containing an extra molecule of 8-quinolinol per molecule of silver chelate. This type of chelate, called a lattice chelate because the extra molecule of 8-quinolinol is thought to be held by weak lattice forces, is known for the 8-quinolinol chelates of Sc, Th, U (VI), and Pu (VI).

Now if the silver 8-quinolinol chelate contains solvated 8-quinolinol, it may be possible to prepare the normal 1:1 chelate by thermal decomposition. To find out whether this is possible, the two modifications of the silver 8-quinolinol chelate were prepared as previously described (*5*) and subjected to thermal decomposition on a thermobalance (*6*).

The thermal decomposition curves for the yellow and green forms of the silver 8-quinolinol chelate are given in Fig. 1. The yellow form was the more stable of the two modifications. It was stable up to 140°C when it began slowly to lose weight. The weight loss then became quite rapid, giving a break in the curve at 280°C; however, a constant weight level having the stoichiometry of the 1:1 chelate was not obtained. Beyond 370°C, further rapid weight loss took place to give the metallic silver level beginning at 505°C.

The green form began to lose weight at 120°C, giving a br[illegible] in the curve at 225°C. Again, a hori[illegible]tal weight level was not found for th[illegible]1:1 chelate. Beyond 415°C, further [illegible]pid weight loss took place to give [illegible] metallic silver level beginning at 600°C.

The results of these curves reveal that it is not possible to remove thermally the extra solvate molecule of 8-quinolinol without total disruption of the silver chelate. Such behavior is contrary to the thermal decomposition of the 8-quinolinol chelates of thorium and uranium (VI) but similar to that of scandium (*7*).

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14 October 1957

Suggested Revision of Nomenclature—Angiotensin

Concurrent discovery has become commonplace, almost as though a mental sputnik regularly circled the earth, distributing with abandon our most exciting thoughts. The vasoactive peptide resulting from the action of renin on an alpha-globulin was thus discovered by two groups of investigators with the result that the peptide received two trivial names, angiotonin and hypertensin. Synthesis of the octapeptide has now brought a degree of certainty about the identity of this peptide and justifies dropping the double nomenclature. We propose the simplified name, *angiotensin*, and its derivatives *angiotensinase* and *angiotensinogen*. *Angiotensin* is a hybrid word but does, we think, have the advantage of being easy to pronounce even with a variety of accents, and it is euphonious and is understandable despite the most recalcitrant microphone.

There will be many who from habit will want no change, but we hope usage will make the heart grow fonder.

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5 December 1957

Book Reviews

A Theory of the Consumption Function. National Bureau of Economic Research, No. 63, General Series. Milton Friedman. Princeton University Press, Princeton, 1957. xvi + 243 pp. $4.75.

Milton Friedman's hypothesis, formulated and, to his own satisfaction at least, demonstrated in *A Theory of the Consumption Function* is twofold: (i) consumption is a function of "permanent" income; and (ii) the ratio of the two does not depend on the *level* of income.

In an opening discussion devoted to pure theory, Friedman essentially sets up a utility function of present against future consumption, specifies (implicitly) that all permanent income is spent over the relevant time period, presumably the lifetime of the individual, and defines permanent income as that amount of receipts the consuming of which leaves wealth intact. Under these conditions, the two major reasons for not spending all receipts in a given period are the desire to straighten out the consumption stream to correspond more closely to the level of permanent income and the desire to earn interest on savings. With an uncertain future, the individual, in making provision against the future, will also tend to vary the fraction of income spent on consumption in accordance with the amount of wealth he owns relative to his income. Friedman goes on to *assume* that the marginal rates of substitution of present against future consumption are homogenous, of degree zero in their ratio—that is, the level of consumption or income has nothing to do with the saving rate. Similarly he assumes that the distribution of individuals by their ability to earn interest, their wealth-income ratios, and their utility functions is independent of their distribution by income. The combination of these two assumptions, the second of which is particularly dubious, yields the proposition that aggregate consumption is a fraction of permanent income which does not vary with the level of income.

The remainder of the book is devoted to demonstrating how two basic sets of empirical data are consistent with the permanent-income hypothesis. Cross-sectional budget studies consistently show a marginal propensity to consume less than the average propensity—that is, an income elasticity of less than one. Yet, over time, the average propensity to consume has been fairly stable. If transitory or temporary income constitutes a larger proportion of measured income among high-income than among low-income groups, then budget studies will show an income elasticity of less than one, even though consumption is a constant fraction of *permanent* income. At the same time, since this fraction is constant, the less-than-one income elasticity of consumption shown in budget studies will not result in a secular change in the average propensity to consume.

Similarly, in aggregate time-series data the permanent-income hypothesis will account for the fact that consumption reacts in a damped way to cyclical changes in income. Since such changes are considered to be in part transitory, and not permanent, consumption adjustments are smaller than income changes. Friedman calculates an aggregate consumption function to fit the time-series data (using a weighted average of past incomes, with weights declining backward in time.)

Friedman's work is indeed a notable contribution to the theory of consumption. His brilliant and subtle exploitation of the data to bolster his hypothesis at many points borders on sheer genius. However, in my judgment the permanent-income hypothesis must be accepted merely as an additional factor shaping consumption behavior. The claim that it is a hypothesis which explains all the major features of consumer behavior must be rejected for a number of reasons.

(1) There is in the book far too much indiscriminate hacking about with Occam's razor (to borrow a phrase of D. H. Robertson). On a number of occasions the reader is urged to accept the hypothesis on the grounds that it is the simplest single explanation of so many empirical facts. Indeed, in this field, any attempt to explain complex human behavior by a simple explanation is automatically suspect.

(2) Aside from some interesting speculations in the first section of chapter III, Friedman finds it quite impossible to formulate an operational definition of permanent income. That consumers do distinguish between windfall changes in income and changes expected to be more permanent is indeed a fruitful intuitional conclusion but hardly a solid enough base on which to build the superstructure which Friedman has erected.

(3) There is no proof whatsoever, in the pure theory section, of the assertion that the fraction of income consumed is independent of the level of income. And any number of hypotheses—for example, positive correlation in budget arrays between wealth-income ratios and income and a stable aggregate wealth-income ratio over time—would account for the failure of consumption to rise secularly at a slower ratio than income. Consequently, Friedman's bold conclusions about savings-income relationships in underdeveloped countries are not warranted either by his theoretical structure or his data.

(4) Friedman's structures against "Keynesian" cyclical analysis are also overdone. At best he merely shows that consumption has a damped response to cyclical changes in income. And indeed his own aggregate function errs in the opposite direction. It sails right through four of the eight consumption downturns since 1905—unlike Dusenberry's function, which catches seven of the eight declines.

(5) Finally, Friedman appears to have proved too much. For if consumption changes only with permanent income, is it not logical that it varies only with permanent changes in real wealth? And if so, one of the major weapons of the "Chicago" quantity theorists against the theory of underemployment equilibrium is seriously weakened. For depression price cuts which raise real wealth balances will surely be regarded, in part at least, as "transitory."

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The Stars above Us. Or the conquest of superstition. Ernst Zinner. Translated by W. H. Johnston. Scribner's, New York, 1957. xiv + 141 pp. Illus. $3.

A dean of historians of astronomy, out of his vast erudition, has brought forth a trivial pamphlet of questionable value, which does not do him justice. This slim volume is not intended as a history of astronomy, nor is it meant to refute astrologers or instruct in modern astron-

omy, although it touches all these subjects. However, the volume is not unworthy of a quick perusal. The author speaks with authority on a number of subjects of interest to an average citizen who, feeling the impact of science, wants to learn something about past attitudes toward science; in spite of its choppy style and structure, this book furnishes a pleasant way to gain such knowledge.

Unfortunately, the book has lost much accuracy and almost all citation of references in the translation. The 125 pages of text are divided into 14 chapters (most of which have numerous subdivisions): "The Sun's Teaching"; "The Host of the Stars" (*sic*) (the German title is "*Das Heer der Sterne*"); "The Dance of the Stars" (which deals with beliefs concerning the moon and the planets and was properly entitled "*Der Reigen der Gestirne*"); "Comets and Portents"; and so on. Some passages bear a strong resemblance to passages Zinner has published elsewhere. Moreover, he has used some of the illustrations before. But gathering together these bits of knowledge to make a new whole is worth while, and the illustrations are delightful and lend much charm.

In the German edition the bibliography is much fuller, each item is numbered, and references by item number and page are frequent in the text. This is not true of the English edition. In both, the bibliography contains many inaccuracies—names misspelled or misabbreviated. This is strange when one reflects that Zinner is the author of an invaluable tool—a bibliography of German astronomical literature during the Renaissance. And why are the title and date of the German edition (*Sternglaube und Sternforschung*, Alber, Freiburg und München, 1953) nowhere stated?

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Pratt Institute, New York

The Vertebrate Visual System. Its origin, structure, and function and its manifestations in disease, with an analysis of its role in the life of animals and in the origin of man. Preceded by a historical review of investigations of the eye, and of the visual pathways and centers of the brain. Stephen Polyak. Heinrich Klüver, Ed. University of Chicago Press, Chicago, 1957. xviii + 1390 pp. Illus. $45.

I should say at once, since this book, more than most, is a highly personal document, that to my great regret my only contact with Stephen Polyak was a hasty handshake outside a waiting elevator. It was general knowledge that he had been dogged by illness through the last years of his life, and that throughout this period he labored ceaselessly to complete this book, the culmination of 30 years of work on the anatomy of the eye and the central nervous system. I gather that in all essentials he succeeded. At his death in 1955 the text, bibliography, and illustrations were complete. However, much remained to be done. That we have the book before us now, we owe largely to Heinrich Klüver's devoted editing. Subsidies from the Public Health Service and National Science Foundation have brought its cost down, within the reach of most libraries. Klüver arranged, corrected, indexed, and ordered, but apparently he subtracted nothing. The book is, in detail, as Polyak wanted it.

It is a very large work: 1390 pages (including 300 pages containing some 10,000 references) and 551 illustrations. Klüver tells us that the legends of the illustrations alone ran to 300 pages of typescript.

The book begins with a history of optics and investigations on the eye and its central nervous connections. Polyak had at his command a wide range of European tongues, ancient and modern, including Slavic, and he has much to say that is of interest in this realm. His historical review is distinguished particularly by its careful appraisal of early Arabic sources.

There follows a detailed examination of the anatomy and histology of the retina and the visual pathways, with particular reference to the primates, including man. This section of over 400 pages is Polyak's particular contribution—the compilation of his life's work. There is no doubt that workers in vision and general neurology will long remain in Polyak's debt for this material, and that, in its wealth of discriminating observation and its beautiful figures, it constitutes a monumental achievement.

There follows a relatively short section of 125 pages on the pathology of the retina and the visual pathways. This is in two parts—a general anatomical discussion and a second, clinical section which contains the description of 12 specific cases involving disturbances of visual field and discussing the underlying pathology.

The book ends with a section of about 300 pages on the origin and development of the vertebrate eye, the natural history and behavior of 11 specific animals, and the role of vision in the origin of man and civilization.

Stephen Polyak was a learned, skilful, resourceful anatomist, and all of us admire and are grateful for his contributions in this field and the devotion with which he pursued it. From his anatomical studies he drew inferences in physiology, paleontology, anthropology, and ethnology. In my opinion, all such excursions ended unhappily. It is possible to infer basic visual physiology from anatomy, as Max Schultze long ago showed, and our classic theory of evolution springs almost wholly from anatomical observations. But this is not where Polyak's gifts lay. The concluding chapter and the strange "Epilogue" have everything in them: a little concerning vision, some genuinely interesting observations in natural history, a great deal that is trivial, and much that is preposterous. I wish that this last section of the book had never been written, or, if written, not published, or, if published, not in a book on vision. It must have given trouble to Klüver, and it will give trouble to any reader aware of Polyak's gifts and accomplishments as a neuroanatomist.

George Wald
Biological Laboratories, Harvard University

Solid State Physics. vol. 4. *Advances in Research and Application.* Frederick Seitz and David Turnbull, Eds. Academic Press, New York, 1957. xiv + 540 pp. Illus. $12.

As in earlier volumes of the series, the excellent articles in this new volume are on widely diverse topics. They are, however, uniformly well written and authoritative and will be very helpful to those wishing to become familiar with new fields. The first article is a comprehensive survey of known facts about ferroelectric and antiferroelectric crystals, by Werner Känzig. The author reviews the present status of theory and the known phenomena in both kinds of materials. Next, the theory of electron mobility in solids is discussed by Frank J. Blatt. The Boltzmann transport equation is used in the study of electric and thermal conductivity, thermoelectric effects, and the Hall effect. After treatment of the simplest possible models, more complicated cases are discussed, including models involving nonspherical energy surfaces and nonisotropic relaxation times.

The next article, by Truman P. Woodruff, is a short discussion of the orthogonalized plane wave method for obtaining electron wave functions in a crystal lattice. The method is carefully described, and its applications by the principal investigators in the field are discussed and compared. There follows a bibliography, by Robert S. Knox, of atomic wave functions. References are given to results for more than 100 atoms and ions, with brief descriptions of the calculations included. The final article discusses techniques of zone melting and crystal growing. This article, by W. G. Pfann, will be of great interest to those who wish to learn of recent advances in these arts.

Arthur F. Kip
University of California, Berkeley

Comprehensive Inorganic Chemistry. vol. 6, *The Alkali Metals,* John F. Suttle; *Hydrogen and Its Isotopes,* Robert [illegible] Brasted. Van Nostrand, Princeton, N.J., 1957. viii + 234 pp. Illus. $6.

Volume 6 of *Comprehensive Inorganic Chemistry* will not disappoint those readers whose familiarity with earlier volumes would lead them to expect a work distinguished by an orderly marshaling of well-chosen data, clearly and concisely interpreted.

These volumes are intended to appeal strongly to the industrial inorganic chemist; part 1, on the alkali metals, places emphasis on industrial processes used in the production of commercially important compounds and on phase diagrams of aqueous and nonaqueous alkali salt systems. Thermodynamics is represented by extensive heat data, although discussion of free energy and entropy is largely lacking. There is very little information on the crystallographic properties of the various salts, and the discussion of organic compounds of the alkalis is limited to two pages. On the other hand, there is a rather surprisingly complete treatment of the behavior of the metals and of various salts in liquid ammonia.

Part 2, devoted to hydrogen and its isotopes, presents an adequate summary of the known thermodynamic and nuclear properties of hydrogen, deuterium, and tritium, as well as a thorough discussion of hydrogen chemistry. Commercially important processes, especially those used for the large-scale preparation of the gas, receive special attention.

Although clearly limited in scope, this volume, like other volumes in the series, is a valuable reference work for anyone working in the field of inorganic chemistry.

B. B. CUNNINGHAM
University of California, Berkeley

The Species Problem. A symposium presented at the Atlanta meeting of the American Association for the Advancement of Science, 28–29 Dec. 1955. Publication No. 50. Ernst Mayr, Ed. American Association for the Advancement of Science, Washington, D.C., 1957. ix + 395 pp. Illus. $8.75; AAAS members, $7.50.

Systematists have good reason to be bored with discussions of the species problem. Nevertheless the problem does exist; it is crucial for all of biological science; and the last word on it has not been and probably never will be said. This symposium achieves novelty by bringing together statements by authors who can discuss the problem with first-hand data but who have not previously generalized from those data in just this context. The authors and their fields are as follows: H. L. Carson, population genetics; V. Grant, botany; J. L. Brooks, limnology; J. Imbrie, paleontology; T. M. Sonneborn, protozoology; J. A. Moore, embryology; and C. L. Prosser, physiology. The editor, Ernst Mayr, has contributed introductory and concluding chapters.

All but one (Sonneborn) of the authors agree with the editor as to the preferred concept of a species. They generally call this the "biological concept," thus perpetuating semantic confusion that has long troubled such discussion. Of course all concepts of species of organisms are *ipso facto* biological. This particular concept is genetical, and indeed genetical in a restricted sense. It is the concept of a species as a population (or group of populations) within which interbreeding commonly occurs but which is well or completely isolated from interbreeding with other populations. The concept has been expressed in many formally different but conceptually identical ways, and it has been discussed for generations and at great length. Restating the concept or merely subscribing to it have long since lost interest. There remain, however, difficulties in its application and questions as to its appropriateness. This symposium demonstrates that discussion of those points still has some value.

When sufficient data are available, this particular genetical concept is usually clear-cut, but it may in numerous instances be vague. That is no argument against use of the concept, because any other runs into at least as many doubtful cases. Yet the lack of a sharply decisive criterion raises problems of practical application. Moreover, the *direct* application of the concept is rarely possible. Its bearing almost always has to be judged from indirect evidence. Those two classes of problems are the principal subjects of the symposium. They are treated by all the authors, perhaps most clearly and extensively by Grant and Imbrie. There are also instances in which use of this concept, directly or indirectly, is theoretically appropriate but may be judged impractical. The one dissident author, Sonneborn, insists that this impracticality is so widespread as to rob the concept of general usefulness. His case is weakened by the fact that his own materials give quite clear-cut results under the very concept that he tends to reject. Apart from that point, Sonneborn's contribution—almost half this volume and really a book in itself— is full of new data and is a major work on some aspects of protozoology.

Let us hope (although it may be too much to hope) that this symposium is the last word on the applicability and practicability of the interbreeding concept of species for organisms that do in fact interbreed. We must look to the future for a truly general solution of the species problem, one that also takes into account the multitude of organisms that do not interbreed.

G. G. SIMPSON
American Museum of Natural History, New York

Vertebrates of the United States. W. Frank Blair, Albert P. Blair, Pierce Brodkorb, Fred R. Cagle, and George A. Moore. McGraw-Hill, New York, 1957. ix + 819 pp. Illus. $12.

The problem of determining biological materials is often formidable and frustrating to the nonspecialist, and any tool that eases the burden is welcome. The present volume is designed to enable anyone to identify, down to species, any vertebrate (except marine fishes and marine turtles) occurring in the United States. It will be used by the nonspecialist, for the specialist on each of the vertebrate groups has at his finger tips the extensive literature of his field. The book is a lineal descendant of Pratt's long-useful *Manual of Land and Fresh Water Vertebrate Animals of the United States,* which has not been available for ten years. This parentage is acknowledged in the preface, and the new book is modeled on its predecessor. The most notable departures are the inclusion of the birds and the parceling out of the sections among several authors.

The sections are not all equally successful. The section on fishes, by G. A. Moore, is excellent. The keys are presented in simple language, intelligible to a nonichthyologist, and characters likely to give trouble are usually illustrated. The sections on amphibians, by A. P. Blair, and on reptiles, by F. R. Cagle, are outstanding. Both are notable for skillful use of illustrations—often simple but effective diagrams—to supplement the wording of the keys. It is difficult for the specialist to appreciate the importance to the nonspecialist of such visual aids. The section on mammals, by W. F. Blair, is somewhat marred by emphasis on the penis bone as a character for many of the smaller rodents. This structure is difficult to prepare, and it is unrealistic to expect a nonspecialist to use it as a character successfully. Fortunately, no identifications depend wholly on characters of the penis bone. Much the weakest section is that on birds, by Pierce Brodkorb, who shows no appreciation of the obvious fact that his chapter will be used almost exclusively by nonornithologists. This section is written largely in the highly private jargon of the ornithol-

ogists, and consequently much is gibberish to anyone else. Illustrations are few and apparently capriciously chosen. Phrases such as "adult downs on apteria only," "secondaries aquintocubital," and "tarsus booted" convey no meaning whatever to me. It is revealing that the vast majority of the words defined in the glossary pertain to birds.

Despite any minor weaknesses, this book should have a long and useful life expectancy. It is a much-needed addition to the everyday working tools of the biologist.

D. Dwight Davis
Chicago Natural History Museum

Modern Applied Photography. G. A. Jones. Philosophical Library, New York, 1957. vi + 162 pp. Plates. $4.75.

This little book provides a bird's-eye view of the whole field of photography as applied in science, industry, and the arts. Photography here means more than "drawing with light"; it means activating any photosensitive surface, with or without the use of conventional cameras, by means of the whole spectrum of energy. There is hardly a field of investigation, an industry, a business, or an art which does not use photography in some sense. Yet people who already use photography would profit from reading this book. Not only would it extend their horizons but it might stimulate the production of new ideas for new applications in their own fields.

The treatment is functional. Chapters deal with photography as an aid to memory, scientific recording, photography by dim and bright light, recording of color, infrared sensitivity, ultraviolet photography, radiography, atomic particles, recording and analysis of motion, photography in production, and photography as an instructor. The bibliography is skimpy; for example, one of the most significant of the new books, published in 1955, is *Research Films in Biology, Anthropology, Psychology, and Medicine,* (Academic Press, New York); it is not listed. The book might well have been enlarged by the inclusion of additional illustrative examples of the processes described. However, this would have increased its cost.

This is a book of principles to stimulate the imagination, not a book of techniques to follow. Anyone using photography professionally (today this includes everyone) can find a flaw in its coverage. I use time-lapse photomicrography in recording the behavior of animal cells in tissue culture. The book discusses time-lapse photography in the study of plant growth and of the movement of clouds, and in the teaching of patterns in ploughing a field, but, alas, does not discuss the cinephotomicrography of cells. Indeed, the author goes out of his way to say that the applications of time-lapse recording are very few; this is not in the spirit of the book, which admirably shows that the applications of photography are many.

Ralph Buchsbaum
University of Pittsburgh

New Books

L'Automatique des Informations. Principes des machines (a calculer, en particulier). Opérant sur de l'information. F.-H. Raymond. Masson, Paris, 1957. 185 pp. Paper, F. 1600.

Human Relations and Power. Sociopolitical analysis and synthesis. Albert Mueller-Deham. Philosophical Library, New York, 1957. 441 pp. $3.75.

The Experimental Control of Plant Growth. With special reference to the Earhart Plant Research Laboratory at the California Institute of Technology. Frits W. Went. Chronica Botanics, Waltham, Mass., 1957 (order from Ronald, New York). 360 pp. $8.50.

Le Volume Sanquin des Poumons Chez l'Homme. Jacques Lammerant. Editions Arscia, Bruxelles, 1957. 192 pp.

Industrial Electronics Handbook. R. Kretzmann. Philips, Eindhoven, Holland; Philosophical Library, New York, 1957 (ed. 1 translated by Harley-Carter, ed. 2 revised by H. E. Kater and D. J. Mitchell). 305 pp. $12.

Industrial Electronics Circuits. R. Kretzmann. Philips, Eindhoven, Holland; Philosophical Library, New York, 1957. Translated by D. J. Mitchell. 202 pp. $10.

Water Waves. The mathematical theory with applications. J. J. Stoker. Interscience, New York, 1957. 595 pp. $12.

Steinsalz und Kalisalze, Franz Lotz. Borntraeger, Berlin, 1957. 477 pp.

Tire Dynamics. Tire marks and their relationship to vehicle velocity prior to brake application. Andrew J. White. Motor Vehicle Research, Inc., South Lee, N.H., 1956. 282 pp.

Chemistry of the Rare Radioelements. Polonium-actinium. K. W. Bagnall. Academic Press, New York; Butterworths, London, 1957. 189 pp. $5.

The Fundamental Constants of Physics. E. Richard Cohen, Kenneth M. Crowe, Jesse W. M. Dumond. Interscience, New York, 1957. 299 pp. $7.50.

Science in Progress. Tenth series. Hugh Taylor, Ed. Yale University Press, New Haven, 1957. 268 pp. $6.50.

Thermodynamics of One-Component Systems. William N. Lacey and Bruce H. Sage. Academic Press, New York, 1957. 387 pp. $8.

Progress Report in Chemical Literature Retrieval. Gilbert L. Peakes, Allen Kent, James W. Perry. Interscience, New York, 1957. 229 pp. $4.75.

Progress in Nuclear Physics. vol. 6. O. R. Frisch, Ed. Pergamon Press, New York and London, 1957. 304 pp. $14.

Nouveau Traité de Chimie Minérale. vol. III. Group 1a, *Rubidium, Césium, Francium*; Group 1b, *Généralités, Cuivre, Argent, Or.* Paul Pascal, Ed. Masson, Paris, 1957. 850 pp. Paper, F. 6000; cloth, F. 6900.

Functional Analysis and Semi-Groups. Colloquium Publ., vol. XXXI. Einar Hille and Ralph S. Phillips. American Mathematical Society, Providence, R.I., rev. ed., 1957. 820 pp. $13.80.

Progress in the Chemistry of Organic Natural Products. vol. XIV. L. Zechmeister, Ed. Springer, Vienna, 1957. 385 pp. $17.85.

Morphology of Plants. Harold C. Bold. Harper, New York, 1957. 692 pp. $8.

Tratado de Doenças das Aves. vol. I, *Doenças Produzidas por virus*; vol. II, *Doenças Produzidas por Bactérias e Fungos*; vol. III, *Doneças Produzidas por Protozoários e Artropódes Parasitas*; vol. IV, *Doenças Produzidas por Helmintos, Doneças da Nutriçao, Donenças dos Orgãos e Aparelhos Vícios, Envenenamentos Patologia do Desenvolvimento Higiene, Terapêutica Geral e Cirúrgica.* J. Reis and P. Nóbrega. Edições Melhoramentos, São Paulo, Brasil, ed. 2, 1957. 1553 pp. (4 vols. bound in two).

The Eye Goddess. O. G. S. Crawford. Macmillan, New York, 1957. 168 pp. $10.

Gazéfication et Oxydation des Combustibles. Bases théoriques et réalisations industrielles de la conversion oxydante. Jacques Meunier. Masson, Paris, 1958. 550 pp. Paper, F. 4500; cloth, F. 5200.

Electron Impact Phenomena. And the properties of gaseous ions. F. H. Field and J. L. Franklin. Academic Press, New York, 1957. 358 pp. $8.50.

The Lipids. Their chemistry and biochemistry. vol. III, *Biochemistry.* Biosynthesis, oxidation, metabolism, and nutritional value. Harry J. Deuel, Jr. Interscience, New York, 1957. 1101 pp. $25.

Encyclopedia of Chemical Technology. First supplement volume. Raymond E. Kirk and Donald F. Othmer, Eds. Interscience, New York, 1957. 992 pp. $25.

Liver: Structure and Function. Hans Popper and Fenton Schaffner. Blakiston Div., McGraw-Hill, New York, 1957. 792 pp. $20.

Van Nostrand's Scientific Encyclopedia. Aeronautics, astronomy, botany, chemical engineering, chemistry, civil engineering, electrical engineering, electronics, geology, guided missiles, mathematics, mechanical engineering, medicine, metallurgy, meteorology, mineralogy, navigation, nuclear science and engineering, photography, physics, radio and television, statistics, zoology. Van Nostrand, Princeton, N.J., ed. 3, 1958. 1846 pp. $30.

Drying Farm Crops. Carl W. Hall. Agricultural Consulting Associates, Reynoldsburg, Ohio, 1957 (order from Edwards, Ann Arbor, Mich.). 359 pp. $7.

Nuclear Radiation in Food and Agriculture. W. Ralph Singleton. Van Nostrand, Princeton, N.J., 1958. 391 pp. $8.50.

The Ashanti. A proud people. Robert A. Lystad. Rutgers University Press, New Brunswick, N.J., 1958. 219 pp. $5.

Does Man Survive Death? A symposium. Eileen J. Garrett, Ed. Helix Press, New York, 1957. 208 pp. $3.75.

An Introduction to the Study of Stellar Structure. S. Chandrasekhar. Dover, New York, 1957. 513 pp. $2.75.

Meetings and Societies

Neutron Interactions with Nuclei

The International Conference on Neutron Interactions with Nuclei, which was held 9–13 September 1957 at Columbia University, New York, N.Y., was attended by 188 American physicists and 57 physicists from 12 other nations. There were representatives from the United Kingdom, Canada, Denmark, Sweden, Norway, the Netherlands, France, Italy, West Germany, Japan, the U.S.S.R., and India. The meeting started with a summary of the present situation in neutron physics, given in a paper by H. A. Bethe (Cornell University), entitled "The Present Status of Neutron Interactions with Nuclei," after which D. J. Hughes (Brookhaven National Laboratory) reviewed the field of low-energy neutron spectroscopy and R. F. Taschek (Los Alamos Scientific Laboratory) reviewed the status of measurements of high-energy neutron cross sections. There were half-day sessions on low-energy neutron spectroscopy, fission physics, the theoretical interpretation of neutron spectroscopy, the process of fission, and fast neutron total and differential cross sections, and there was a session on the gamma rays emitted after neutron capture.

An impressive development in the field of low-energy neutron spectroscopy was the vast quantity of data available from the multichannel time analyzers now in use in this field. As an example of this, L. J. Rainwater (Columbia University) presented results obtained with a multichannel analyzer in which 2000 points were taken simultaneously to produce a full curve of the neutron cross section versus energy all at one time. Large quantities of data obtained with the many 1000-channel analyzers in use throughout the world were also presented. With regard to the design and performance of experiments and the accumulation of data, the situation in this field is quite healthy.

Unfortunately, the situation with respect to the theory of the interactions of slow neutrons with nuclei is not as good, although significant progress has been made. However, it is still not possible to use the theory of the process to calculate with confidence results where experimental data do not exist.

The cloudy-crystal-ball model of the nucleus, in which the nucleus is assumed to be a sphere which can reflect and absorb neutrons, has been modified by changing the sphere to an ellipsoid. With this change, the calculated strength of the neutron interaction varies with the number of particles in the nucleus in a somewhat different way from what it does for a spherical nucleus, and the results calculated from the ellipsoidal nucleus agree much better with the experimental results than do those calculated on the basis of the spherical nucleus.

The ellipsoidal theory of the nucleus has been applied thus far only to low-energy neutrons where the neutron cannot change the total orbital angular momentum of the nucleus. Resonance levels in which the orbital angular momentum of the nucleus is unchanged are called S levels; those in which the nucleus is changed by 1 quantum $h/2\pi$ are called p levels; by 2 quanta, d levels; by 3 quanta, f levels, and so on. It is now clear experimentally that levels other than S levels must be taken into consideration in fitting theoretical curves to low-energy neutron data. It has now been clearly demonstrated experimentally by H. Newson (Duke University) that the density of resonance levels is proportional to $(2J+1)$, where J is the angular momentum of the compound nucleus.

Even though large quantities of experimental data are available on neutron resonances, more data must be accumulated and the theory must be improved considerably before one can calculate with confidence the cross section of any isotope at a particular energy or, for that matter, even the average cross section over a broad energy region.

In general, fission physics is in a much worse state than is neutron spectroscopy because of the great difficulties in the areas of both experiment and theory. Even though the experimental results have improved considerably in the last two years, there is still no self-consistent set of cross sections available. The fission cross section of uranium-235, which we would think would be the most accurately known because of its economic importance in reactor technology, is a subject of argument among the numerous physicists who have performed measurements of this quantity. Different results disagree by more than 16 percent, even though the accuracy of the measurement is thought to be about 2 percent.

The situation with respect to the resonance levels in the fissionable nuclei is even worse. It is usually possible to assume that all resonance levels in a particular nucleus are independent and thus to determine the parameters of the level independently. For the resonances of fissionable nuclei, each resonance seems to be connected in some way to the resonance next to it, and thus the problem of analysis becomes much more complicated.

Looked at from the theoretical point of view, the fission process can be assumed to occur through many different channels or through just a few. These channels have now been identified, in Bohr's collective model, with the levels in the transition state nucleus, whose angular momenta and parity correspond to the parameters of the compound nuclear levels formed by the capture of a neutron. If fission can occur through only a few channels, then one expects to find that the resonance levels are connected with one another, but if it can occur through a large number of channels, then the levels should be independent. It is now clear from the experimental results that the number of channels allowable is fairly small. In the case of uranium-233, the number appears to be 1; in that of plutonium-239, it is probably 1; but in that of uranium-235, the present data are not yet self-consistent. It is also clear that the quantum mechanical barrier penetration is a useful concept in explaining qualitatively the character of the fission process, but the details of fission are certainly not well explained.

In fast-neutron physics it was clear that the spherical, cloudy-crystal-ball model of the nucleus could fit the gross aspects of the experimental results at energies below a few million electron volts but that it certainly does not fit in detail. In particular, H. H. Barschall (University of Wisconsin) presented a paper showing that the present cloudy-crystal-ball theory did not fit the results of his experiments with polarized neutrons. Theoretical results in which a spin orbit coupling was introduced were also presented at the conference, to take account of polarization, but the theoretical calculations did not agree with the experimental results. Although the theory is probably capable of taking these effects into consideration, considerably more work must be done, both theoretically and experimentally, before the situation is well understood. It was generally agreed that studies of polarized neutrons are a wide-open field.

Many of the new significant experimental results came from the application of two relatively new techniques to neutron spectroscopy. The two techniques

are (i) the use of 100-percent efficient detectors with extremely large liquid scintillators and (ii) the fast-neutron time-of-flight technique. The application of these techniques has made it possible to do experiments that were conceived many years ago but languished unperformed because their execution was then beyond the hopes of even the wildest dreamer.

The application of the time-of-flight technique to measurements of inelastic scattering of neutrons has produced some clear data which can be compared with theory. Previously, the data available with the older techniques were very sparse, and no general check of the theory could be made. An excellent review of some of the older techniques and of the data obtainable was presented by Joan Freeman (Harwell, England). In this field the theorist is well ahead of the experimentalist. Most of the experimental results are well explained by existing theory. Considerably more experimental data must be accumulated in order to fill out the theory and check its more critical points, but in general the situation is satisfactory.

The application of the 100-percent efficient liquid scintilla[tor] was beautifully demonstrated by J. [Cor]rell (Los Alamos), who measured [the] distribution of the number of neutron[s] emitted when a nucleus fissions, and [by] B. Diven (Los Alamos), who directly measured capture cross sections—a measurement which was previously possible only for nuclei which resulted in a relatively long-lived radioactive isotope.

The results of a large number of experiments with fast neutrons in which all available techniques were used pointed up one of the current controversies in the theory of nuclear reactions—namely, direct interaction versus compound nucleus. According to the direct interaction theory, a particle reacts with only one particle in the nucleus, whereas, according to the compound nucleus theory, a particle is absorbed by the nucleus and loses its identity completely, and then the excited nucleus gets rid of its excess energy by some process which has nothing to do with the way in which the compound nucleus was formed. It is now clear that, in the energy region up to a few million electron volts, compound nucleus formation is predominant. However, at higher energies the situation is not clearly understood, and the process that actually takes place is probably a combination of both direct interaction and compound nucleus formation.

One fact that emerged in the discussion was that many people had been interpreting their data erroneously. Compound nucleus theory predicts that the angular distribution of particles emitted by the compound nucleus should be symmetrical about 90°, whereas direct interaction theory predicts that the angular distribution should be peaked in the forward direction. When the experimental results showed that the results were not symmetrical about 90°, the results were interpreted in terms of direct interaction. At the conference several people pointed out that it was possible to have angular distributions which were not symmetrical about 90° without an interpretation of direct interaction being required. If the statistical assumption that many levels are involved in an observed cross section is not valid, then it is possible to have interference between nearby levels that would destroy the symmetry about 90°. Reinterpretation of experimental results, with more careful attention to the interference process, should give us a better idea of how the nuclear reactions proceed. Thus, we must study angular distributions as a function of the energy of the incident particle to see how the nuclear reaction changes from compound nucleus formation at low energies to direct interaction at higher energies, since it is clear that the reaction process goes principally by direct interaction at very high energies.

The final session of the meeting dealt with the gamma rays emitted after neu-

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January 31, 1958

TO RESEARCH DIRECTORS

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tron capture and in the reverse process—a topic which has long been neglected in the study of neutron interactions with nuclei. In this session G. A. Bartholomew (Chalk River, Canada) summarized the situation in this field and pointed out that significant results can be obtained with much higher resolution in order to separate various levels and determine the level structure. L. V. Grochev (Academy of Sciences of the U.S.S.R.) reported some of his results, obtained by means of a high-resolution gamma ray spectrometer. He showed how significant results could be obtained. He was able to interpret his results for the light elements in terms of direct capture of a neutron into shell model states. In heavy even-even nuclei, the existence of rotational bands at an energy around 1 Mev was inferred from the existence of strong γ-ray lines of about this energy. (Capture is about 8 Mev, and the shell and collective model have usually only been successful in exploring levels near the ground state of the nucleus.)

H. Schultz (Yale University) presented some results on the energy distribution of gamma rays, from neutrons captured by a particular neutron resonance, and B. Trumpy (Kjeller, Norway) presented results of polarization measurements. Both of these techniques promise to give some information on the spins of levels. The extension and refinement of these techniques promise to give a wealth of new experimental information and a more fundamental understanding of the capture process in terms of nuclear models.

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Forthcoming Events

March

1. Junior Solar Symposium, Tempe, Ariz. (Association for Applied Solar Energy, 3424 N. Central Ave., Phoenix, Ariz.)

1–3. National Wildlife Federation, St. Louis, Mo. (E. F. Swift, NWF, 232 Carroll St., NW, Washington 12.)

3. Wildlife Soc., annual, St. Louis, Mo. (D. L. Leedy, U.S. Fish and Wildlife Service, Washington 25.)

5–6. Gas Conditioning Conf., 7th annual, Norman, Okla. (M. L. Powers, Extension Div., Univ. of Oklahoma, Norman.)

6–8. Fundamental Cancer Research, 12th annual, Houston, Tex. (W. K. Sinclair, M. D. Anderson Hospital and Tumor Inst., Univ. of Texas, Houston 25.)

9–14. International College of Surgeons, 11th biennial cong., Los Angeles, Calif. (K. A. Meyer, 1516 Lake Shore Dr., Chicago 10, Ill.)

10–13. American Assoc. of Petroleum Geologists, annual, Los Angeles, Calif. (R. H. Dott, AAPG, Box 979, Tulsa 1, Okla.)

10–13. Society of Economic Paleontologists and Mineralogists, annual, Los Angeles, Calif. (R. H. Dott, Box 979, Tulsa, Okla.)

16–21. Nuclear Engineering and Science Cong., Chicago, Ill. (D. I. Cooper, *Nucleonics,* 330 W. 42 St., New York.)

17–21. National Assoc. of Corrosion Engineers, 14th annual, San Francisco, Calif. (NACE, Southern Standard Bldg., Houston 2, Tex.)

18–20. Amino Acids and Peptides, Ciba Foundation symp. (by invitation), London, England. (G. E. W. Wolstenholme, 41 Portland Pl., London, W.1.)

20–22. Michigan Acad. of Science, Arts and Letters, annual, Ann Arbor. (R. F. Haugh, Dept. of English, Univ. of Michigan, Ann Arbor.)

20–22. Pulmonary Circulation Conf., Chicago, Ill. (Wright Adams, Chicago Heart Assoc., 69 W. Washington St., Chicago 2.)

20–23. International Assoc. for Dental Research, annual, Detroit, Mich. (D. Y. Burrill, Northwestern Univ. Dental School, 311 E. Chicago Ave., Chicago 11, Ill.

23–26. American Assoc. of Dental Schools, annual, Detroit, Mich. (M. W. McCrea, 42 S. Greene St., Baltimore 1, Md.)

(See issue of 24 January for comprehensive list)

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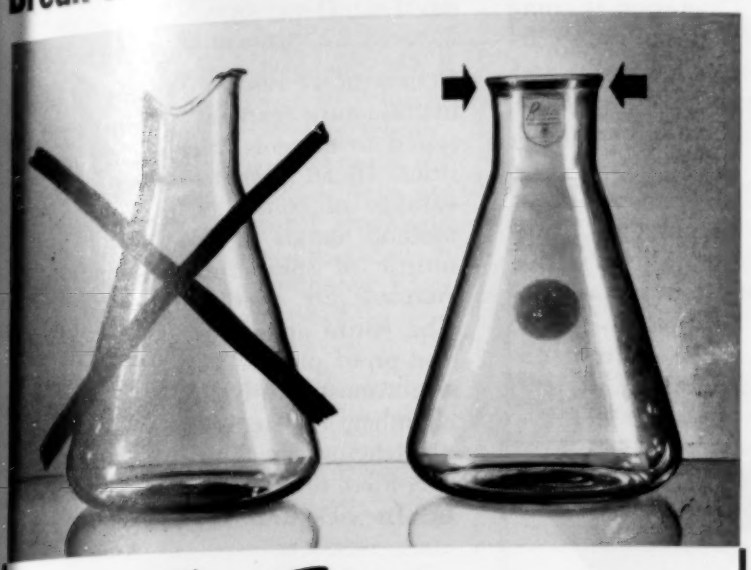

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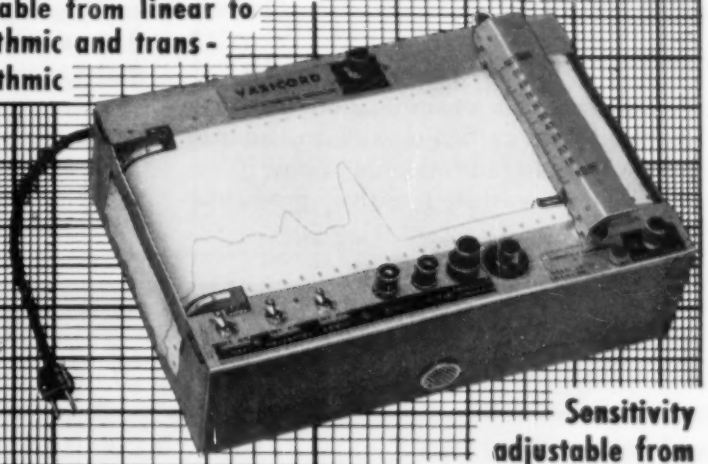

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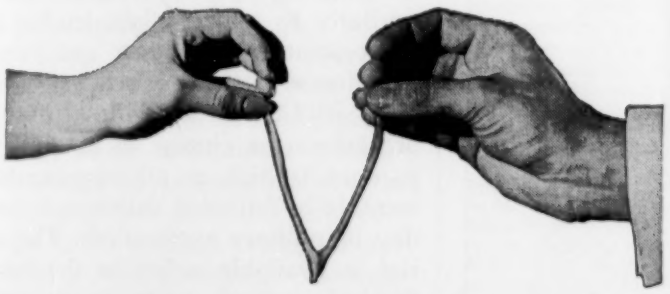

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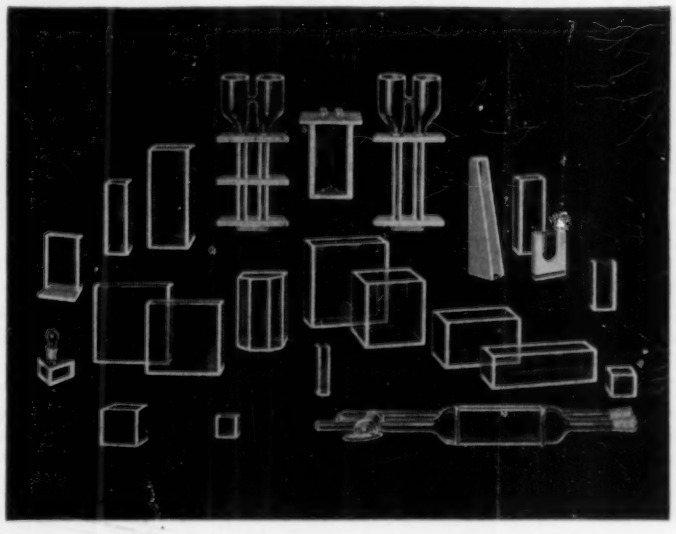

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EQUIPMENT NEWS

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■ STERILIZER uses a combination of ethylene oxide and carbon dioxide to sterilize finished packaged material as well as heat- and moisture-sensitive products. The gas is said to penetrate sealed cardboard, polyvinyl, or paper containers to sterilize the contents. Operation is completely automatic. All phases of the sterilization cycle are indicated visually and recorded on a two-pen pressure-temperature graph. (Wilmot Castle Company, Dept. S852)

■ HYGROGRAPH uses a diaphragm of animal membrane as the humidity-sensitive element. Sensitivity of 1 percent and accuracy ±3 percent are said to be achieved. Operating range is from 15- to 95-percent relative humidity at temperatures from 32° to 130°F. Humidity is recorded on a 12 by 6 in. chart. (Servdex Inc., Dept. S875)

■ CORROSION TEST CHAMBER of Swiss manufacture exposes materials to be tested to aerosols of constant characteristics. In addition to providing the advantage of controlled particle size, the method avoids the air currents characteristic of sprays produced by nozzles. Aerosols are produced by disc rotors. The entire apparatus is made of corrosion-proof plastic. To prevent the corrosive atmosphere from escaping from the chamber, the aerosols are entrapped in air leaving the apparatus in Raschig-ring-filled flues. (Spectrographic Specialties Inc., Dept. S867)

■ PULSE MODULATOR tests high-power pulse tranformers by simulating actual operating conditions. Transformers having ratings up to 30 Mw peak, and 60 kw average power, may be tested. Banks of pulse-forming components may be selected by means of patch-cord connections to produce pulses of from 0.5- to 8-μsec duration. Repetition frequency is continuously variable from 50 to 1800 pulses per second. Maximum duty cycle is 0.002. Peak pulse output is 200 kv into 1300 ohm. (Manson Laboratories, Inc., Dept. S865)

■ SELENIUM GLASS transmits infrared radiation to 25 μ. The material handles similarly to optical glass, lending itself to conventional molding and polishing techniques. Rigidity is retained after 15 hr at 70°C, with no evidence of optical breakdown or change in power. Transparency is high at all wavelengths detectable by infrared detectors in use today in military applications. The material is available either in the form of finished optical parts or as molded blanks. (Eastman Kodak Co., Dept. S869)

■ UNIVERSAL BRIDGE provides facilities for two-, three-, or four-terminal measurements of impedance or transfer admittance at operating frequency of 1592 cy/sec. Ranges covered are: capacitance, 0.0002 μμf to 11 μf in seven ranges; conductance, 10^{-1} to 10^{-8} mho, in seven ranges; inductance, 1 mh to infinity in seven ranges. Measurement is not affected by the impedance of the test leads. A low-impedance adapter provides four additional ranges. (Robertshaw-Fulton Controls Co., Dept. S872)

■ SOLENOID DEWAR FLASKS are designed for study of the effect of magnetic fields on properties of materials at liquid-helium temperatures. A variety of sizes and of materials of construction are available. (Hofman Laboratories, Dept. S878)

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